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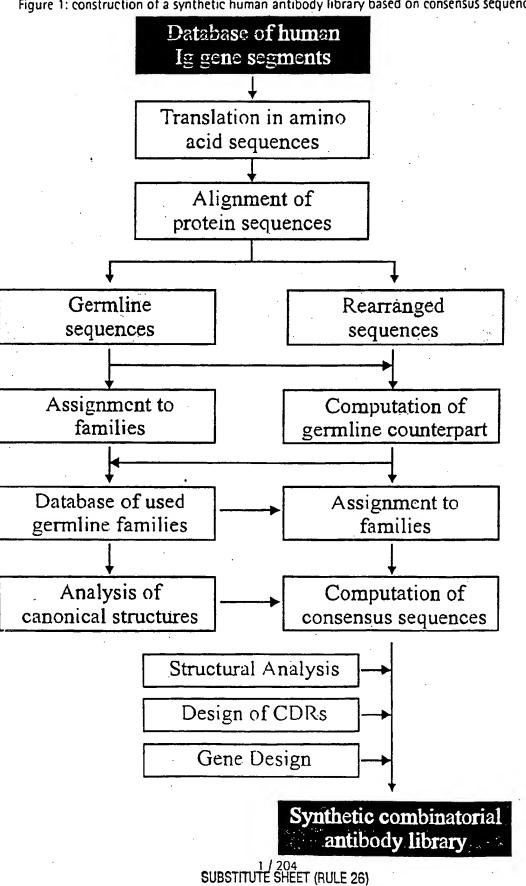
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Figure 1: construction of a synthetic human antibody library based on consensus sequences



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Figure 2A: VL kappa consensus sequences

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Figure 2B: VL lambda consensus sequences

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Figure 2B: VL lambda consensus sequences

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GCTCTGGATC CGTTTTAGCG TGCAAAGCGG GGTCCCGTCC GCCAGCAGCT

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Figure 3B: V kappa 2 (Vk2) gene sequence

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Figure 38: V kappa 2 (Vk2) gene sequence (continued)

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Figure 3C: V kappa 3 (Vk3) gene sequence (continued)

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Figure 3D: V kappa 4 (Vĸ4) gene sequence

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Figure 3D: V kappa 4 (Vx4) gene sequence (continued)

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igure 4A: V lambda 1 (Vλ.1) gene sequence Q S V L T Q P P S V S G A P S S S S S S S S S S S S	CAGAGCGTGC TGACCCAGCC GCCTTCAGTG AGTGGCGCAC GTCTCGCACG ACTGGGTCGG CGGAAGTCAC TCACCGCGTG Eco57I	V T I S C S G S S N I G BSSSI	TGTGACCATC TCGTGTAGCG GCAGCAGCAG CAACATTGGC	Z Q	TGAGCTGGTA CCAGCAGTTG CCCGGGACGG CGCCGAAACT ACTCGACCAT GGTCGTCAAC GGGCCCTGCC GCGGCTTTGA	DNNQRPSGVPDRF: Bsu361	

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GATAACAACC AGCGTCCCTC AGGCGTGCCG GATCGTTTTA GCGG
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Figure 4A: V lambda 1 (VA.1) gene sequence (continued)

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Figure 4B: V lambda 2 (Vλ2) gene sequence	Q	CAC	H	CA1 GT2	\succ	ATC TAC	>	TATGATGTGA ATACTACACT
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Figure 4B: V

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Figure 4C: V lambda 3 (VA3) gene sequence

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Figure 4C: V lambda 3 (VA.3) gene sequence (continued)

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Figure 5A: V heavy chain 1A (VH1A) gene sequence	>	CAGGTGCAAT TGGTTCAGTC GTCCACGTTA ACCAAGTCAG	V K	CGTGAAAGTG GCACTTTCAC	S	TTAGCTGGGT GCGCCAAGCC AATCGACCA CGCGGTTCGG	I I P I F G T ATTATTCCGA TTTTGGCAC TAATAAGGCT AAAAACCGTG	V T BstEII
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Figure 5A: V heavy chain 1.A (VH1A) gene sequence (continued)

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Figure 5B: V heavy chain 1B (VH1B) gene sequence

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Figure 58: V heavy chain 18 (VH18) gene sequence (continued)	1B (V)	41B) gen	ie segi) aouar	continu	(pa	•								
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Figure 5C: V heavy chain 2 R T, T	heavy	chain T	n 2 (VH2) gene sequence (continued) T S K D T	ည်း လ	I S K D T S K N O V L T			ഗ	×		z	0	>	>	П	H	
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Figure 5D: V heavy chain 3 (VH3) gene sequence

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Figure 5D: V heavy chain 3 (VH3) gene sequence (continued)

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SUBSTITUTE SHEET (RULE 26)

Figure 5E: V heavy chain 4 (VH4) gene sequence

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Figure 5E: V heavy chain 4 (VH4) gene sequence (continued)

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Figure 5F: V heavy chain 5 (VH5) gene sequence	L V Q S G A E V K K P G E S		₹	TGGTTCAGAG	ACCAAGTCTC
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3 Ø П K Н S ഗ Figure 5F: V heavy chain 5 (VH5) gene sequence (continued) \bowtie Ø ഗ \vdash BStEII CTTCAATGGA GAAGTTACCT GTGGCGCATA CACCGCGTAT TTTCGTAATC AAAGCATTAG AGCGCGGATA TCGCGCCTAT CCACTGGTAA GGTGACCATT

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V S S BlpI GGTTAGCTCA CCAATCGAGT

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Figure 5G: V heavy chain 6 (VH6) gene sequence

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CGAGTGGCTG GCTCACCGAC CCGCACCGGA GGCGTGGCCT CTGGATTCGC CAGTCTCCTG GTCAGAGGAC GACCTAAGCG CGGCGTGGAA GCCGCACCTT

CGGTGAGCGT GCCACTCGCA ഗ > K TTGCTAATAC AACGATTATG Y O Z CAAATGGTAT GTTTACCATA 3 GCCCTACCT ATTATCGTAG CCGCCATGGA TAATAGCATC ∝ . T

CAGTTTAGCC GTCAAATCGG ~~~~ BSSHII S استا Ø TGGGCCTATG AAGCTTTTTG TTCGAAAAAC Z > ~ ~ ~ ~ ~ ~ ~ NspV EagI Ø ഗ E ACCCGGATAC Е Ω 回 Figure 5G: V heavy chain 6 (VH6) gene sequence (continued) Д Д Z ATTACCATCA TAATGGTAGT ⊱ BsaBI > ₽ S GAAAAGCCGG CTTTTCGGCC Z 召 Н ഗ Ø 又 П

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CCTGGTGACG GTTAGCTCAG GGACCACTGC CAATCGAGTC

- Figure 6: oligonucleotides for gene synthesis
- **O1K1** 5'- GAATGCATACGCTGATATCCAGATGACCCAGAG-CCCGTCTAGCCTGAGC -3'
- **O1K2** 5'- CGCTCTGCAGGTAATGGTCACACGATCACCCAC-GCTCGCGCTCAGGCTAGACGGC -3'
- **01K3** 5'- GACCATTACCTGCAGAGCGAGCCAGGGCATTAG-CAGCTATCTGGCGTGGTACCAGCAG -3'
- **01K4** 5'- CTTTGCAAGCTGCTGCTGCATAAATTAATAGT-TTCGGTGCTTTACCTGGTTTCTGCTGGTACCACGCCAG -3'
- **O1K5** 5'- CAGCCAGCAGCTTGCAAAGCGGGGTCCCGTCCC-GTTTTAGCGGCTCTCGGATCCGGCACTGATTTTAC -3'
- O1K6 5'- GATAATAGGTCGCAAAGTCTTCAGGTTGCAGGC-TGCTAATGGTCAGGGTAAAATCAGTGCCGGATCC -3'
- **O2K1** 5'- CGATATCGTGATGACCCAGAGCCCACTGAGCCT-GCCAGTGACTCCGGGCGAGCC -3'
- **O2K2** 5'- GCCGTTGCTATGCAGCAGGCTTTGGCTGCTTCT-GCAGCTAATGCTCGCAGGCTCGCCCGGAGTCAC -3'
- O2K3 5'- CTGCTGCATAGCAACGGCTATAACTATCTGGAT-TGGTACCTTCAAAAACCAGGTCAAAGCCC -3'
- **O2K4** 5'- CGATCCGGGACCCCACTGGCACGGTTGCTGCCC-AGATAAATTAATAGCTGCGGGCTTTGACCTGGTTTTTG -3'
- **O2K5** 5'- AGTGGGGTCCCGGATCGTTTTAGCGGCTCTGGA-TCCGGCACCGATTTTACCCTGAAAATTAGCCGTGTG -3'
- **O2K6** 5'- CCATGCAATAATACACGCCCACGTCTTCAGCTT-CACACGCCTAATTTTCAGGG -3'
- O3K1 5'- GAATGCATACGCTGATATCGTGCTGACCCAGAG-CCCGG -3'
- O3K2 5'- CGCTCTGCAGCTCAGGGTCGCACGTTCGCCCGG-AGACAGGCTCAGGGTCGCCGGGCTCTGGGTCAGC -3'
- O3K3 5'- CCCTGAGCTGCAGAGCGAGCCAGAGCGTGAGCA-GCAGCTATCTGGCGTGGTACCAG -3'

Figure 6: (continued)

- O3K4 5'- GCACGGCTGCTCGCGCCATAAATTAATAGACGCGGTGCTTGACCTGGTTCTGCTGGTACCACGCCAGATAG -3'
- O3K5 5'- GCGCGAGCAGCCGTGCAACTGGGGTCCCGGCGC-GTTTTAGCGGCTCTGGATCCGGCACGGATTTTAC -3'
- O3K6 5'- GATAATACACCGCAAAGTCTTCAGGTTCCAGGC-TGCTAATGGTCAGGGTAAAATCCGTGCCGGATC -3'
- **04K1** 5'- GAATGCATACGCTGATATCGTGATGACCCAGAG-CCCGGATAGCCTGGCG -3'
- **04K2** 5'- GCTTĆTGCAGTTAATGGTCGCACGTTCGCCCAG-GCTCACCGCCAGGCTATCCGGGC -3'
- **04K3** 5'- CGACCATTAACTGCAGAAGCAGCCAGAGCGTGC-TGTATAGCAGCAACAACAAAAACTATCTGGCGTGGTACCAG 3'
- **O4K4** 5'- GATGCCCAATAAATTAATAGTTTCGGCGGCTGA-CCTGGTTTCTGCTGGTACCACGCCAGATAG -3'
- **O4K5** 5'- AAACTATTAATTTATTGGGCATCCACCCGTGAA-AGCGGGGTCCCGGATCGTTTTAGCGGCTCTGGATCCGGCAC-3'
- **O4K6** 5'- GATAATACACCGCCACGTCTTCAGCTTGCAGGG-ACGAAATGGTCAGGGTAAAATCAGTGCCGGATCCAGAGCC -3'
- **O1L1** 5'- GAATGCATACGCTCAGAGCGTGCTGACCCAGCC-GCCTTCAGTGAGTGG -3'
- **O1L2** 5'- CAATGTTGCTGCTGCTGCCGCTACACGAGATGG-TCACACGCTGACCTGGTGCGCCACTCACTGAAGGCGGC -3'
- **O1L3** 5'- GGCAGCAGCAGCAACATTGGCAGCAACTATGTG-AGCTGGTACCAGCAGTTGCCCGGGAC -3'
- **O1L4** 5'- CCGGCACGCCTGAGGGACGCTGGTTGTTATCAT-AAATCAGCAGTTTCGGCGCCGTCCCGGGCAACTGC -3'
- **O1L5** 5'- CCCTCAGGCGTGCCGGATCGTTTTAGCGGATCC-AAAAGCGGCACCAGCGCGAGCCTTGCG -3'

Figure 6: (continued)

- o1L6 5'- CCGCTTCGTCTTCGCTTTGCAGGCCCGTAATCG-CAAGGCTCGCGCTGG -3'
- **O2L1** 5'- GAATGCATACGCTCAGAGCGCACTGACCCAGCC-AGCTTCAGTGAGCGGC -3'
- **O2L2** 5'- CGCTGCTAGTACCCGTACACGAGATGGTAATGC-TCTGACCTGGTGAGCCGCTCACTGAAGCTGG -3'
- **O2L3** 5'- GTACGGGTACTAGCAGCGATGTGGGCGGCTATA-ACTATGTGAGCTGGTACCAGCAGCATCCCGG -3'
- **O2L4** 5'- CGCCTGAGGGACGGTTGCTCACATCATAAATCA-TCAGTTTCGGCGCCTTCCCGGGATGCTGCTGGTAC -3'
- **O2L5** 5'- CAACCGTCCCTCAGGCGTGAGCAACCGTTTTAG-CGGATCCAAAAGCGGCAACACCGCGAGCC -3'
- **O2L6** 5'- CCGCTTCGTCTTCCGCTTGCAGGCCGCTAATGG-TCAGGCTCGCGGTGTTGCCG -3'
- **O3L1** 5'- GAATGCATACGCTAGCTATGAACTGACCCAGCC-GCCTTCAGTGAGCG -3'
- O3L2 5'- CGCCCAGCGCATCGCCGCTACACGAGATACGCG-CGGTCTGACCTGGTGCAACGCTCACTGAAGGCGGC -3'
- **O3L3** 5'- GGCGATGCGCTGGGCGATAAATACGCGAGCTGG-TACCAGCAGAAACCCGGGCAGGCGC -3'
- O3L4 5'- GCGTTCCGGGATGCCTGAGGGACGGTCAGAATC-ATCATAAATCACCAGAACTGGCGCCTGCCCGGGTTTC -3'
- **O3L5** 5'- CAGGCATCCCGGAACGCTTTAGCGGATCCAACA-GCGGCAACACCGCGACCCTGACCATTAGCGG -3'
- O3L6 5'- CCGCTTCGTCTTCCGCCTGAGTGCCGCTAATGG-TCAGGGTC -3'
- O1246H1 5'- GCTCTTCACCCCTGTTACCAAAGCCCAG-GTGCAATTG -3'
- **O1AH2** 5 ' GGCTTTGCAGCTCACTTTCACGCTGCTGCCCGG-TTTTTTCACTTCCGCGCCAGACTGAACCAATTGCACCTGGGC-TTTG -3'

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Figure 6: (continued)

O1AH3 5 '- GAAAGTGAGCTGCAAAGCCTCCGGAGGCACTTT-TAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCCTGGGCAGGCTC -3'

- **O1AH4** 5 '- GCCCTGAAACTTCTGCGCGTAGTTCGCCGTGCC-AAAAATCGGAATAATGCCGCCCATCCACTCGAGACCCTGCCC-AGGGGC -3 '
- **O1AH5** 5 '- GCGCAGAAGTTTCAGGGCCGGGTGACCATTACC-GCGGATGAAAGCACCAGCACCGCGTATATGGAACTGAGCAGCCTGCG -3 '
- **Olabh6** 5'- GCGCGCAATAATACACGGCCGTATCTTCGCT-ACGCAGGCTGCTCAGTTCC -3'
- **01BH2** 5 ' GGCTTTGCAGCTCACTTTCACGCTCGCGCCCGG-TTTTTTCACTTCCGCGCCGCTCTGAACCAATTGCACCTGGGC-TTTG -3'
- **01BH4** 5 '- GCCCTGAAACTTCTGCGCGTAGTTCGTGCCGCC-GCTATTCGGGTTAATCCAGCCCATCCACTCGAGACCCTGCCCAGGGGC -3 '
- **01BH5**5'- GCGCAGAAGTTTCAGGGCCGGGTGACCATGACC-CGTGATACCAGCATTAGCACCGCGTATATGGAACTGAGCAGCCTGCG -3'
- **O2H2** 5'- GGTACAGGTCAGGGTCAGGGTTTGGGTCGGTTT-CACCAGGGCCGGCCGCTTTCTTTCAATTGCACCTGGGCTTTG-3'
- **02H3** 5'- CTGACCCTGACCTGTACCTTTTCCGGATTTAGC-CTGTCCACGTCTGGCGTTGGCGTGGGCTGGATTCGCCAGCCGCCTGGGAAAG -3'
- **O2H4** 5'- GCGTTTTCAGGCTGGTGCTATAATACTTATCAT-CATCCCAATCAATCAGAGCCAGCCACTCGAGGGCTTTCCCAGGCGCTGG -3'

Figure 6: (continued)

- **O2H5** 5'- GCACCAGCCTGAAAACGCGTCTGACCATTAGCA-AAGATACTTCGAAAAATCAGGTGGTGCTGACTATGACCAACAT
- **02H6** 5'- GCGCGCAATAATAGGTGGCCGTATCCACCGGGT-CCATGTTGGTCATAGTCAGC -3'
- O3H1 5'- CGAAGTGCAATTGGTGGAAAGCGGCGGCCT-GGTGCAACCGGGCGGCAG -3'
- O3H2 5'- CATAGCTGCTAAAGGTAAATCCGGAGGCCGCGC-AGCTCAGACGCAGGCTGCCGCCCGGTTGCAC -3'
- O3H3 5'- GATTTACCTTTAGCAGCTATGCGATGAGCTGGG-TGCGCCAAGCCCCTGGGAAGGGTCTCGAGTGGGTGAG -3'
- O3H4 5'- GGCCTTTCACGCTATCCGCATAATAGGTGCTGC-CGCCGCTACCGCTAATCGCGCTCACCCACTCGAGACCC -3'
- **O3H5** 5'- CGGATAGCGTGAAAGGCCGTTTTACCATTTCAC-GTGATAATTCGAAAAAACACCCTGTATCTGCAAATGAACAG-3'
- O3H6 5'- CACGCGCGCAATAATACACGGCCGTATCTTCCG-CACGCAGGCTGTTCATTTGCAGATACAGG -3'
- **04H2** 5'- GGTCAGGCTCAGGGTTTCGCTCGGTTTCACCAG-GCCCGGACCACTTTCTTGCAATTGCACCTGGGCTTTG -3'
- **O4H3** 5'- GAAACCCTGAGCCTGACCTGCACCGTTTCCGGA-GGCAGCATTAGCAGCTATTATTGGAGCTGGATTCGCCAGCCGC-3'
- **O4H4** 5'- GATTATAGTTGGTGCTGCCGCTATAATAAATAT-AGCCAATCCACTCGAGACCCTTCCCAGGCGGCTGGCGAATCCAGG-3'
- **O4H5** 5'- CGGCAGCACCAACTATAATCCGAGCCTGAAAAG-CCGGGTGACCATTAGCGTTGATACTTCGAAAAACCAGTTTAGCCTG -3'
- **O4H6** 5'- GCGCGCAATAATACACGGCCGTATCCGCCGCCG-TCACGCTGCTCAGGTTTCAGGCTAAACTGGTTTTTCG -3'

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Figure 6: (continued)

O5H1 5'- GCTCTTCACCCCTGTTACCAAAGCCGAAGTGCA-ATTG -3'

- **O5H2** 5'- CCTTTGCAGCTAATTTTCAGGCTTTCGCCCGGT-TTTTTCACTTCCGCGCCGCTCTGAACCAATTGCACTTCGGCTTTGG -3'
- **O5H4** 5'- CGGAGAATAACGGGTATCGCTATCGCCCGGATA-AATAATGCCCATCCACTCGAGACCCTTCCCAGGCATCTGGCGCAC -3'
- **O5H5** 5'- CGATACCCGTTATTCTCCGAGCTTTCAGGGCCA-GGTGACCATTAGCGCGGATAAAAGCATTAGCACCGCGTATCTTC-3'
- **O5H6** 5'- GCGCGCAATAATACATGGCCGTATCGCTCGCTT-TCAGGCTGCTCCATTGAAGATACGCGGTGCTAATG -3'
- **O6H2** 5'- GAAATCGCACAGGTCAGGCTCAGGGTTTGGCTC-GGTTTCACCAGGCCCGGACCAGACTGTTGCAATTGCACCTGG-GCTTTG -3'
- **O6H3** 5'- GCCTGACCTGTGCGATTTCCGGAGATAGCGTGA-GCAGCAACAGCGCGGCGTGGAACTGGATTCGCCAGTCTCCTGGGCG-3'
- **O6H4** 5'- CACCGCATAATCGTTATACCATTTGCTACGATA-ATAGGTACGGCCCAGCCACTCGAGGCCACGCCCAGGAGACTG-GCG -3'
- **O6H5** 5'- GGTATAACGATTATGCGGTGAGCGTGAAAAGCC-GGATTACCATCAACCCGGATACTTCGAAAAACCAGTTTAGCCTGC -3'
- **O6H6** 5'- GCGCGCAATAATACACGGCCGTATCTTCCGGGG-TCACGCTGTTCAGTTGCAGGCTAAACTGGTTTTTC -3'
- OCLK15'- GGCTGAAGACGTGGGCGTGTATTATTGCCAGCA-GCATTATACCACCCGCCGACCTTTGGCCAGGGTAC -3'

Figure 6: (continued)

- OCLK25'- GCGGAAAAATAAACACGCTCGGAGCAGCCACCG-TACGTTTAATTTCAACTTTCGTACCCTGGCCAAAGGTC -3'
- OCLK3 5'- GAGCGTGTTTATTTTTCCGCCGAGCGATGAACA-ACTGAAAAGCGGCACGGCGAGCGTGGTGTCCTGCTG -3'
- OCLK4 5 ' CAGCGCGTTGTCTACTTTCCACTGAACTTTCGC-TTCACGCGGATAAAAGTTGTTCAGCAGGCACACCACGC -3 '
- OCLK5 5'- GAAAGTAGACAACGCGCTGCAAAGCGGCAACAG-CCAGGAAAGCGTGACCGAACAGGATAGCAAAGATAG -3'
- OCLK6 5 ' GTTTTTCATAATCCGCTTTGCTCAGGGTCAGGG-TGCTGCTCAGAGAATAGGTGCTATCTTTGCTATCCTGTTCG 3 '
- OCLK75'- GCAAAGCGGATTATGAAAAACATAAAGTGTATG-CGTGCGAAGTGACCCATCAAGGTCTGAGCAGCCCGGTG -3'
- OCLK8 5 ' GGCATGCTTATCAGGCCTCGCCACGATTAAAAG-ATTTAGTCACCGGGCTGCTCAGAC -3 '
- OCH1 5'- GGCGTCTAGAGGCCAAGGCACCCTGGTGACGGTTAGCTCAGCGTCGAC -3'
- © 32 5'- GTGCTTTTGCTGCTCGGAGCCAGCGGAAACACG-CTTGGACCTTTGGTCGACGCTGAGCTAACC -3'
- OCH3 5'- CTCCGAGCAGCAAAAGCACCAGCGGCGCACGG-CTGCCCTGGGCTGCCTGGTTAAAGATTATTTCC -3'
- **OCH4** 5'- CTGGTCAGCGCCCCGCTGTTCCAGCTCACGGTG-ACTGGTTCCGGGAAATAATCTTTAACCAGGCA -3'
- OCH5 5'- AGCGGGGCGCTGACCAGCGGCGTGCATACCTTT-CCGGCGGTGCTGCAAAGCAGCGGCCTG -3'
- OCH6 5'- GTGCCTAAGCTGCTCGGCACGGTCACAACG-CTGCTCAGGCTATACAGGCCGCTGCTTTGCAG -3'
- OCH7 5'- GAGCAGCAGCTTAGGCACTCAGACCTATATTTG-CAACGTGAACCATAAACCGAGCAACACC -3'
- OCH8 5'- GCGCGAATTCGCTTTTCGGTTCCACTTTTTAT-CCACTTTGGTGTTGCTCGGTTTATGG -3'

Figure 7A: sequence of the synthetic Ck gene segment

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GCGATGAACA CGCTACTTGT TTTCCGCCGA AAAGGCGGCT GCACAAATAA CGTGTTTATT GACGAGGCTC CTGCTCCGAG GCATGCCACC CGTACGGTGG

AACTTTTATC TTGAAAATAG GGACGACTTG GCGTGGTGTG CCTGCTGAAC CCGTGCCGCT CGCACCACAC > > S GGCACGGCGA Ø ₽ G ACTGAAAAGC TGACTTTTCG ഗ ×

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GCACCTATTC CGTGGATAAG ഗ TCGTTTCTAT AGCAAAGATA Ω × ഗ CGAACAGGAT GCTTGTCCTA Ω Ø 团 AAAGCGTGAC TTTCGCACTG > ഗ 回 AACAGCCAGG TTGTCGGTCC Ø ഗ

AAACATAAAG TTTGTATTTC CCTAATACTT GGATTATGAA H Ω ACCCTGACCC TGAGCAAAGC TGGGACTGGG ACTCGTTTCG Ø × ഗ Н H TCTGAGCAGC AGACTCGTCG Ŋ ഗ

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Figure 7A: sequence of the synthetic Ck

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TCTTTTAATC GTGGCGAGGC CTGATAAGCA TGC AGAAAATTAG CACCGCTCCG GACTATTCGT ACG

Figure 7B: sequence of the synthetic CH1 gene segment

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AGGCTCGTCG TCCGAGCAGC AAGGCGACCG TICCGCIGGC GGTTCGCACA CCAAGCGTGT CTGGTTTCCA GACCAAAGGT CGAGTCGCAG GCTCAGCGTC

TTAAAGATTA CCGACGGACC AATTTCTAAT X > GGCTGCCTGG C L G GGCTGCCCTG CCGACGGGAC A L Ø GCGCCGCCAC CGCCGCCGTG ග : ტ ഗ TTTTCGTGGT AAAAGCACCA E ഗ

CTGACCAGCG GACTGGTCGC ⊱ GICGCCCCCC CAGCGGGGCG <u>ග</u> ഗ Z TGAGCTGGAA ACTCGACCTT Z ഗ > GGTCAGTGGC CCAGTCACCG ⊣ Д TTTCCCGGAA AAAGGGCCTT 띠 Д لتا

GTATAGCCTG CATATCGGAC ഗ GTGCTGCAAA GCAGCGGCCT CGTCGCCGGA Ŋ ഗ ഗ CACGACGTTT Ø 口 CTTTCCGGCG GAAAGGCCGC Ø Д GCGTGCATAC CGCACGTATG 工 > U

TTAGGCACTC AGACCTATAT TCTGGATATA Ø AATCCGTGAG [-U GAGCAGCAGC CTCGTCGTCG ഗ ഗ ACTGGCACGG TGACCGTGCC Д > \vdash > TCGTCGCAAC AGCAGCGTTG > ഗ

Figure 7B: sequence of the synthetic CH1 gene segment (continued)

K K V AAAAAGTGG TTTTTCACC GTTTCACCTA CAAAGTGGAT AACCATAAAC CGAGCAACAC GCTCGTTGTG Z · ഗ Д TTGGTATTTG X 工 TTGCAACGTG AACGTTGCAC Z \circ

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AACCGAAAAG CGAATTCTGA TAAGCTT TTGGCTTTTC GCTTAAGACT ATTCGAA

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Figure 7C: functional map and sequence of module 24 comprising the synthetic CA gene segment (huCL lambda)

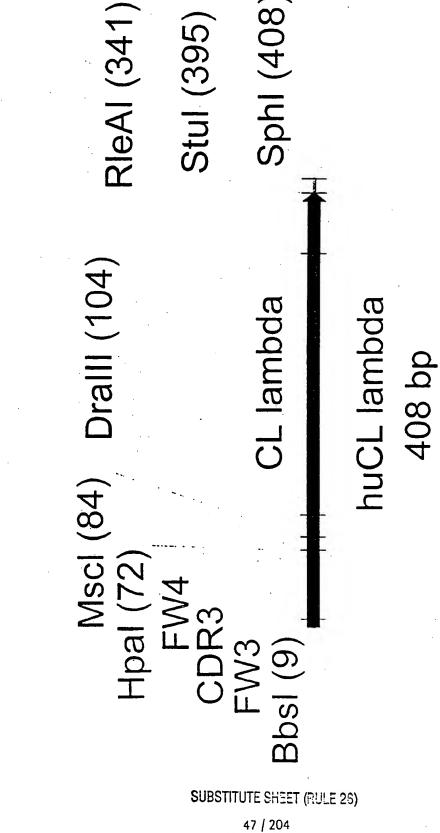


Figure 7C: functional map and sequence of module 24 comprising the synthetic CI gene segment (huCL lambda) (continued)

| CA CCCGGCCTGT                             | MscI<br>~~~~~~<br>TGGCCAGCCG AAAGCCGCAC<br>ACCGGTCGGC TTTCGGCGTG | A GGCGAACAAA<br>ST CCGCTTGTTT                                        | NG CCGTGACAGT            | GCCCCGTCAA GGCGGGAGTG GAGACCACCA |
|-------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------|--------------------------|----------------------------------|
| CATTATACCA<br>GTAATATGGT                  | •                                                                | AAGAATTGCA<br>TTCTTAACGT                                             | TATCCGGGAG<br>ATAGGCCCTC | GGCGGGAGT                        |
| TTGCCAGCAG                                | HPAI<br>~~~~~~<br>GGCACGAAGT TAACCGTTCT<br>CCGTGCTTCA ATTGGCAAGA | GCTGTTTCCG CCGAGCAGCG AAGAATTGCA<br>CGACAAAGGC GGCTCGTCGC TTCTTAACGT | TAGCGACTTT<br>ATCGCTGAAA | GCCCCGTCAA                       |
| CGGATTATTA<br>GCCTAATAAT                  | HpaI<br>~~~~~~<br>GGCACGAAGT TAACCGTTCT<br>CCGTGCTTCA ATTGGCAAGA | GCTGTTTCCG<br>CGACAAAGGC                                             | TGTGCCTGAT<br>ACACGGACTA | GCAGATAGCA                       |
| BDS1<br>~~~~~<br>GAAGACGAAG<br>CTTCTGCTTC | GTTTGGCGGC                                                       | Dralii<br>~~~~~~<br>CGAGTGTGAC<br>GCTCACACTG                         | GCGACCCTGG<br>CGCTGGGACC | GGCCTGGAAG                       |
| <b>-</b>                                  | 51                                                               | 101                                                                  | 151                      | 201                              |

Figure 7C: functional map and sequence of module 24 comprising the synthetic Cl gene segment (huCL lambda) (continued)

CTATCTGAGC GATAGACTCG CGGCCAGCAG GCCGGTCGTC AACAAGTACG TTGTTCATGC ACAAAGCAAC TGTTTCGTTG CACCCTCCAA GTGGGAGGTT 251

RleAI

AGCTACAGCT GTCCCACAGA AGCAGTGGAA CTGACGCCTG

301

GCCAGGTCAC CGGTCCAGTG TCGATGTCGA CAGGGTGTCT TCGTCACCTT GACTGCGGAC

StuI

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GAGGCCTGAT CTCCGGACTA ACGCGGCTGA TGCGCCGACT AAAAAACCGT TTTTTGGCA AGCACCGTGG TCGTGGCACC

SphI

~ ~ ~ ~

AAGCATGC TTCGTACG 401

GCATGAGGGG

351

CGTACTCCCC

Figure 7D: oligonucleotides used for synthesis of module M24 containing CA gene segment

M24: assembly PCR

M24-A: GAAGACAAGCGGATTATTATTGCCAGCAGCATTATACCACCCCGCCTGTGTTTGGCGGCG-

GCACGAAGTTAACCGTTC

M24-B: CAATTCTTCGCTGCTCGGCGGAAACAGCGTCACACTCGGTGCGGCTTTCGGCTGGCCAA-

GAACGGTTAACTTCGTGCCGC

M24-C: CGCCGAGCAGCGAAGAATTGCAGGCGAACAAAGCGACCCTGGTGTGCCTGATTAGCGACT-

TTTATCCGGGAGCCGTGACA

M24-D: TGTTTGGAGGGTGTGGTCTCCACTCCCGCCTTGACGGGGCTGCTATCTGCCTTCCAG-

GCCACTGTCACGGCTCCCGG

M24-E: CCACACCCTCCAAACAAAGCAACAAGAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGC-

CTGAGCAGTGGAAGTCCCACAGAAGCTACAGCTG

M24-F: GCATGCTTATCAGGCCTCAGTCGGCGCAACGGTTTTTCCACGGTGCTCCCCTCATGCGT-

GACCTGGCAGCTGTAGCTTC

H Com the fact that the H H H H. H B. And the state of the state of the state of

Д Н Figure 8: sequence and restriction map of the synthetic gene encoding the consensus single-chain fragment VH3-VK2 Sapi 口 Н Н Ø Ц Ø Н Н S O^l × Σ

AGAAGTGGGG TCTTCACCCC TTACCGTTGC AATGGCAACG TGACCGTGAG GCACTATTGC ACTGGCACTC CGTGATAACG ATGAAACAAA TACTTTGTTT

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GAAAGCGGCG CTTTCGCCGC CGTTAACCAC GCAATTGGTG TTCTACTTCA AAGATGAAGT GCCGACTACA CGGCTGATGT TGTTACCAAA ACAATGGTTT

BSPEI Ø Ø C ഗ Ц K П ഗ G C Д Ø > Н G

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GCGCCGGAGG CGCGGCCTCC GGCAGCCTGC GTCTGAGCTG CAGACTCGAC CCGTCGGACG CGTTGGCCCG GCAACCGGGC GCGGCCTGGT CGCCGGACCA

BstXI Ø Q K > 3 S Σ ď × ഗ ഗ Ľ Н BspEI بتا ഗ

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CCTAAATGGA AATCGTCGAT ACGCTACTCG ACCCACGCGG TTCGGGGACC

TGCGATGAGC TGGGTGCGCC AAGCCCCTGG

GGATTTACCT TTAGCAGCTA

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Figure 8: sequence and restriction map of the synthetic gene encoding the consensus single-chain fragment VH3-Vk2 (continued) ഗ G C ഗ Ċ S ß > 3 ഠ XhoI U

GGCAGCACCT CCGTCGTGGA GCCATCGCCG CGGTAGCGGC CGCGCTAATC GCGCGATTAG CTCACCCACT GAGTGGGTGA GAAGGGTCTC CTTCCCAGAG

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TGATAATTCG ACTATTAAGC CCATTTCACG GGTAAAGTGC GGCCGTTTTA CCGGCAAAAT TAGCGTGAAA ATCGCACTTT TAATACGCCT ATTATGCGGA

K EagI AAGATACGGC Н 口 CTGCGTGCGG K K Н AAAAACACCC TGTATCTGCA AATGAACAGC S Z Σ Ø Н \succ П Н Z NspV ×

TTCTATGCCG

GACGCACGCC

TTACTTGTCG

ACATAGACGT

TTTTTGTGGG

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GCGATGGATT TGCGCGCGTT GGGGCGCGA TGGCTTTTAT CGTGTATTAT

Ineuce aud	2	5	Figure 8: sequence and restriction map of the synthetic gene encoding the consensus single-chain fragment VH3-VK2 (continued)	ap of t	he synthe	tic gene	: encodi	ng the c	onsens	sus single	-chain	fragm	ent VH3-V	'K2 (cor	tinued)
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 \mathtt{EcoRV} Ω S C r C G S C C Ŋ C S G U G C

GTTCCGATAT CAAGGCTATA CCGCCACCAC GGCGGTGGTG GCCACCAAGA CGGTGGTTCT CCTCGCCACC GGAGCGGTGG GGGGGGGTG CCGCCGCCAC

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GGCGAGCCTG CCGCTCGGAC AGTGACTCCG TCACTGAGGC ACTCGGACGG TGAGCCTGCC GTCTCGGGTG CAGAGCCCAC GCACTACTGG CGTGATGACC

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CAACGGCTAT GTTGCCGATA TGCTGCATAG ACGACGTATC AGCCAAAGCC TCGGTTTCGG CTGCAGAAGC GACGTCTTCG CGAGCATTAG GCTCGTAATC

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K P G Q S P Q L L SexAI AAACCA GGTCAAAGCC CGCAGCTATT	Q K P G Q S P Sexal TCAAAAACCA GGTCAAAGCC	L Q K P G Q S P Sexal ~ CT TCAAAAACCA GGTCAAAGCC	Y L Q K P G Q S P pnI SexAI TACCT TCAAAAACCA GGTCAAAGCC	W Y L Q K P G Q S P KpnI SexAI TGGTACCT TCAAAAACCA GGTCAAAGCC	N Y L D W Y L Q K P G Q S P KpnI SexAI
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K P G C Sexal 	Q K P G Ç SexAI T TCAAAAACCA GGTCA	L Q K P G Ç Sexai ~ ~~~~~~ CT TCAAAAACCA GGTCA	Y L Q K P G Ç pnI SexAI TACCT TCAAAAACCA GGTCA	W Y L Q K P G Ç KpnI SexAI TGGTACCT TCAAAAACCA GGTCA	N Y L D W Y L Q K P G C KpnI AACTATCTGG ATTGGTACCT TCAAAAACCA GGTCA
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K 5	Q K E TCAAAAAC	L Q K 2 CT TCAAAAAC	Y L Q K pnI TACCT TCAAAAAC	W Y L Q K KpnI	N Y L D W Y L Q K KpnI AACTATCTGG ATTGGTACCT TCAAAAAC
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D W Y L KpnI	D W Y KpnI ~~~~~~	D W K K ~~~	D AT		N Y AACTATC
L D W Y L KpnI	L D W Y KpnI ~~~~~	L D W K ~~	L D	L	N N AACT
Y L D W Y L KpnI ATCTGG ATTGGTACCT	Y L D W Y KpnI ~~~~~	Y L D W K K ~~	N Y L D AACTATCTGG AT	Y L	

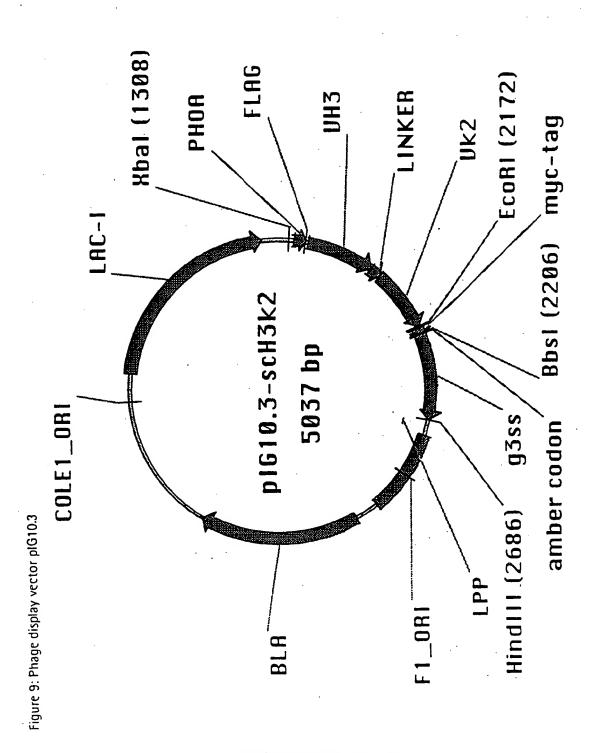
TGTGGAAGCT ACACCTTCGA TTTAATCGGC AAATTAGCCG TTTACCCTGA AAATGGGACT GCCGTGGCTA CGGCACCGAT CGAGACCTAG GCTCTGGATC

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GGGCGGCTG CCCGCCGAC CATTATACCA GTAATATGGT TTGCCAGCAG AACGGTCGTC GCGTGTATTA CGCACATAAT GAAGACGTGG CTTCTGCACC

Figure 8: sequence and restriction map of the synthetic gene encoding the consensus single-chain fragment VH3-VK2 (continued)					
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quence	Ŋ	MscI	1 1 1	GGC	CCG
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Figure 10: Sequence analysis of initial libraries

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Figure 10: Sequence analysis of initial libraries

Figure 11: Expression analysis of initial library



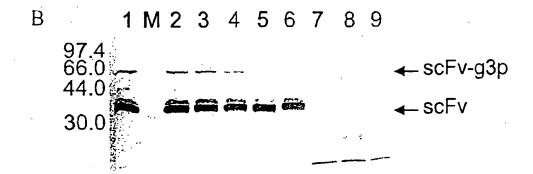
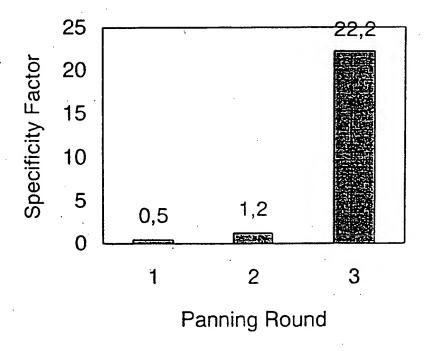


Figure 12: Increase of specificity during the panning rounds

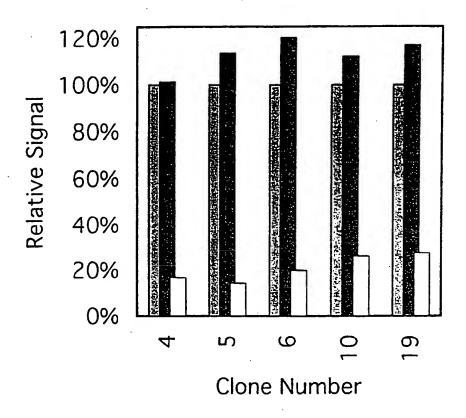


10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 Figure 13: Phage ELISA of clones after the 3rd round of panning 6 ∞ 9 \mathcal{L} 7. 6. 9. 6. 0 wusota (0.04) substitute sheet (Rule 26) 1,5

Clone Number

WO 97/08320 PCT/EP96/03647

Figure 14: Competition ELISA



- No Inhibition
- Inhibition with BSA
- ☐ Inhibition with Fluorescein

Figure 15: Sequence analysis of fluorescein binders

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Figure 16: Purification of fluorescein binding scFv fragments

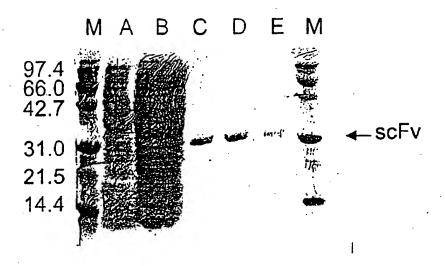
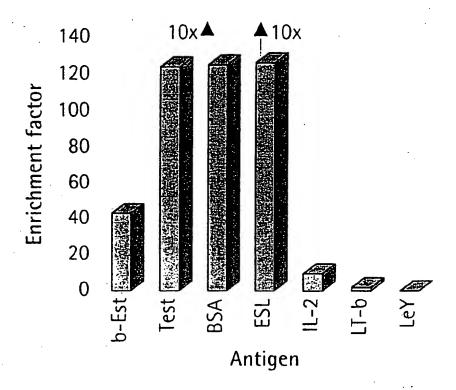


Figure 17: Enrichment factors after three rounds of panning



anti-B-estradiol antibodies D4-6 anti-ESL-1 antibodies 9.0 0.8 0.2 0.4 0 Jay-(mugo+)00 SUBSTITUTE SHEET (RULE 26) 66 / 204

Figure 18: ELISA of anti-ESL-1 and anti-B-estradiol antibedies

Figure 19: Selectivity and cross-reactivity of HuCAL antibodies

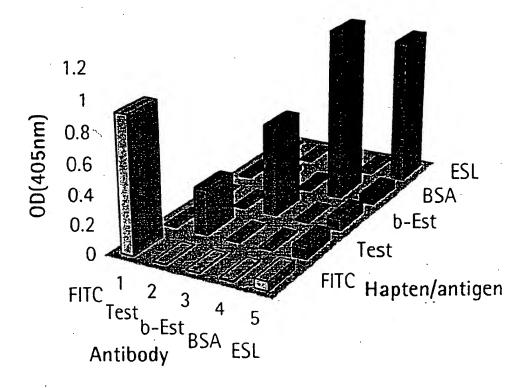


Figure 20: Sequence analysis of estradiol binders

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Figure 21

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Figure 22: Sequence analysis of lymphotoxin-B binders

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Figure 23: Sequence analysis of ESL-1 binders

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Figure 24: Sequence analysis of BSA binders

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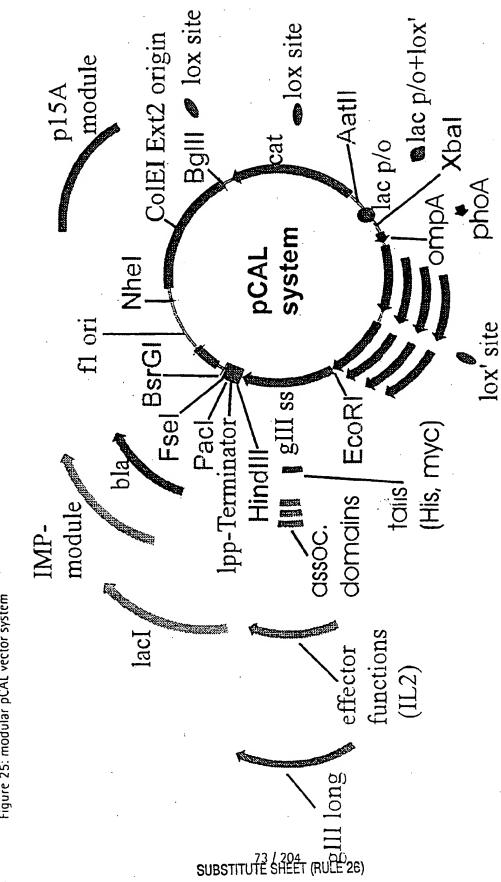


Figure 25: modular pCAL vector system

Figure 25a: List of unique restriction sites used in or suitable for HuCAL genes or pCAL vectors

unique restriction site	Isoschizomers
Aatil	/
AfIII	Bfrl, BspTl, Bst981
Ascl	/
Asel	Vspl, Asnl, PshBl
BamHI	Bstl
Bbel	Ehel, Kasl, Narl
Bbsl	BpuAl, Bpil
BgIII	j
Blpl	Bpu1102I,CellI, BlpI
BsaBl	Maml, Bsh1365l, BsrBRl
BsiWl	Pfl23II, SplI, Sunl
BspEl	AccIII, BseAI, BsiMI, Kpn2I, Mrol
BsrGl	Bsp1407l, SspBl
BssHII	Paul
BstEll	BstPl, Eco91l, Eco0651
BstXI	
Bsu36l	Aocl, Cvnl, Eco811
Dralll	- 1
DsmAl	
Eagl	BstZI, EclXI, Eco52I, XmaIII
Eco571	
Eco01091	Drall
EcoRI	
EcoRV	Eco32l
Fsel	<u> </u>
HindIII	1
Hpal	1
Kpnl	Acc651, Asp7181
Mlul	
Mscl	Ball, MluNl

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Figure 25a: List of unique restriction sites used in or suitable for HuCAL genes or pCAL vectors

unique restriction site	Isoschizomers
Munl	Mfel
Nhel	1
Nsil	Ppu10l, EcoT22l, Mph1103l
NspV	Bsp119l, BstBl, Csp45l, Lspl, Sful
Pacl	I
Pmel	1
PmII	BbrPl, Eco72I, PmaCl
Psp5II	PpuMI
Pstl	
Rsrll	(Rsril), Cpol, Cspl
SanDl	
Sapi	1
SexAl	1
Spel	
Sfil	
Sphl	Bbul, Pael,Nspl
Stul	Aatl, Eco147l
Styl	Eco130l, EcoT14l
Xbal	BspLU11II
Xhol	PaeR7I
Xmal	Aval, Smal, Cfr91, PspAl

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WO 97/08320	•			PCT/EP96/0364
reference	Skerra et al. (1991) Bio/Technology 9, 273-278	Hoess et al. (1986) Nucleic Acids Res. 2287-2300	see M2	Ge et al., (1994) Expressing antibodies in E. coli. In: Antibody engineering: A practical approach. IRL Press, New York, pp 229-266
template	vector pASK30	(synthetic)	(synthetic)	vector plG10
sites to be inserted	Aatli	lox, BgIII	lox', Sphl	none
sites to be removed	2x Vspl (Asel)	2x Vspl (Asel)	none	Sphl, BamHl
functional element	lac promotor/opera or	Cre/lox recombination site	Cre/lox' recombination site	glllp of filamentous phage with N- terminal myctail/amber codon
module/flan-king restriction sites	AatII-lacp/o- Xbal	BgIII-lox- Aatli	Xbal-lox'- Sphl	EcoRI- gIIIlong- HindIII
0N	M1	M2	M3	M7-1

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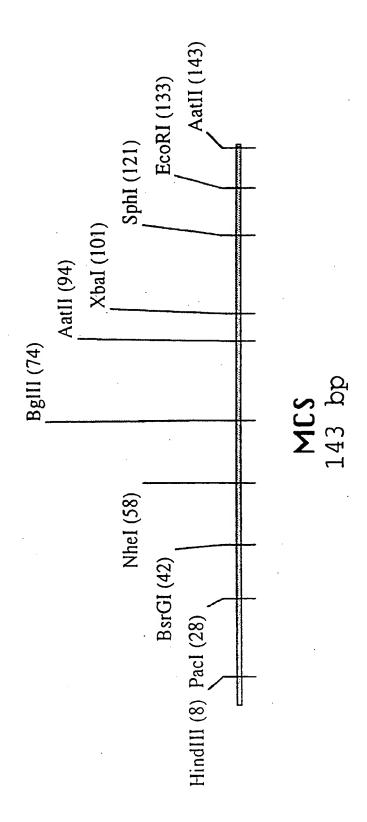
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	see M7-1	see M7-1	see M3	see M1	see M1	see M1	see M1
	vector plG10	vector plG10	(synthetic)	(synthetic)	pASK30	pASK30	pASK30
			lox	Pacl, Fsel	Pacl, Fsel, BsrGl	BsrGI, Nhel	BsrGl, Nhel
	Sphl	Sphl, Bbsl	none	none	Vspl, Eco571, BssSl	Dralll (Banll not removed)	DrallI, BanlI
modules	truncated gillp of filamentous phage with N-termina Gly- Ser linker	truncated gillp of filamentous phage with N-terminal myctail/amber codon	Cre/lox recombination site	lpp-terminator	beta-lactamase/bla (ampR)	origin of single- stranded replication	origin of single- stranded replication
Figure 26: list of pCAL vector modules	EcoRI-gIIIss- HindIII	M7-III EcoRI-gIIIss- HindIII	Sphl-lox- HindIII	HindIII-Ipp- Pacl	M10- Paci/Fsel-bla- II BsrGl	M11- BsrGI-f1 ori-	BsrGI-f1 ori- Nhel
Figure 2	M7-11	M7-III	M8	M9-11	M10-	M11-	M11-

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	WO 97/0832	20	· · · · · ·			PCT/EP96
	Rose, R.E. (1988) Nucleic Acids Res. 16, 355	see M3	Yanisch-Peron, C. (1985) Gene 33,103-119	Cardoso, M. & Schwarz,S. (1992) J. Appl. Bacteriol.72, 289-293	see M1	Knappik, A & Plückthun, A. (1994) BioTechniques 17, 754-761
·	pACYC184	(synthetic)	pUC19	pACYC184	(synthetic)	(synthetic)
	Nhel, BgIII	BgIII, lox, Xmnl	Bgill, Nhel			
	BssSI, VspI, NspV	none	Eco571 (BssSl not removed)	BspEI, MscI, Styl/Ncol	(synthetic)	(synthetic)
r modules	origin of double- stranded replication	Cre/lox recombination site	origin of double- stranded replication	chloramphenicol- acetyltransferase/ cat (camR)	signal sequence of phosphatase A	signal sequence of phosphatase A + FLAG detection tag
Figure 26: list of pCAL vector modules	Nhel-p15A- BgIII	BgIII-lox- BgIII	BgIII-ColEI- Nhel	Aatll-cat- BgIII	Xbal-phoA- EcoRI	Xbal-phoA- FLAG-EcoRI
Figure 2	M12	M13	M14- Ext2	M17	M19	M20

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	Lee et al. (1983) Infect. Immunol. 264-268	see M1	Lindner et al., (1992) Methods: a companion to methods in enzymology 4, 41-
	(synthetic)	pASK30	(synthetic)
	(synthetic)	BstXI, MluI,BbsI, BanII, BstEII, HpaI, BbeI, VspI	(synthetic)
modules	heat-stable enterotoxin II signal (synthetic) sequence	lac-repressor	poly-histidine tail
Figure 26: list of pCAL vector modules	Xbal-stll- Sapl	AfIII-laci- Nhei	EcoRI-Histail- HindIII
Figure 2	M21	M41	M42
		Our	

Figure 27: functional map and sequence of MCS module



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Figure 27: functional map and sequence of MCS module (continued)

BSrGI	CCCCCCCCC TGTACACCCC GGGGGGGG ACATGTGGGG	Aatii Xbai	CCCCCCCGA CGTCCCCCCT GGGGGGGCT GCAGGGGGGA	EcoRI AatII	CCCCCGCATG CCCCCCCCC CGAATTCGAC GTC GGGGGGGGGGGGG GCTTAAGCTG CAG
PacI	CCTTAATTAA GGAATTAATT	BgllI	CCAGATCTCC GGTCTAGAGG	· ·	9999999999
II.	TTCCCCCCCC AAGGGGGGGG	· · · · · · · · · · · · · · · · · · ·	999999999 ၁၁၁၁၁၁၁၁၁	Sphi	CCCCCGCATG
HindI	ACATGTAAGC TGTACATTCG	NheI	CCCCCCGCTA	XbaI	CTAGACCCCC GATCTGGGGG
			51		0.1

Figure 28: functional map and sequence of pMCS cloning vector

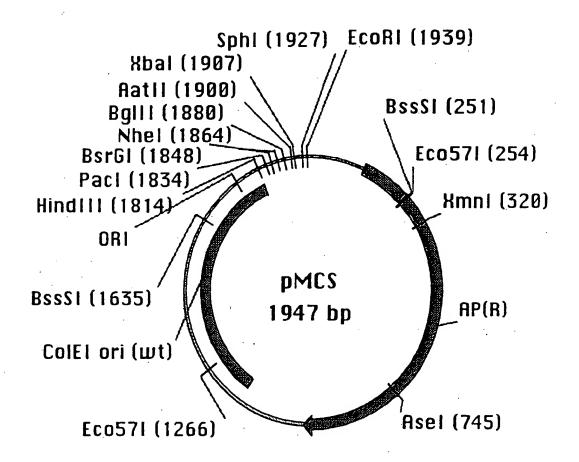


Figure 28: fur 1	Figure 28: functional map and sequence of pMCS cloning vector (continued) 1 CAGGTGGCAC TTTTCGGGGA AATG	of pMCS cloning vector (c TTTTCGGGGA	ontinued) AATGTGCGCG	GAACCCCTAT	TTGTTTATTT	
	GTCCACCGTG	AAAAGCCCCT	TTACACGCGC	CTTGGGGATA	AACAAATAAA	
27	TTCTAAATAC AAGATTTATG	АТТСАААТАТ ТААĞТТТАТА	GTATCCGCTC CATAGGCGAG	ATGAGACAAT TACTCTGTTA	AACCCTGATA TTGGGACTAT	
101	AATGCTTCAA TTACGAAGTT	TAATATTGAA ATTATAACTT	AAAGGAAGAG TTTCCTTCTC	TATGAGTATT ATACTCATAA	CAACATTTCC GTTGTAAAGG	
151	GTGTCGCCCT	TATTCCCTTT ATAAGGGAAA	TTTGCGGCAT	TTTGCCTTCC AAACGGAAGG	TGTTTTTGCT ACAAAAACGA	
201	CACCCAGAAA GTGGGTCTTT	CGCTGGTGAA GCGACCACTT	AGTAAAAGAT TCATTTTCTA	Eco57I ~~~~~~ GCTGAAGATC CGACTTCTAG	AGTTGGGTGC TCAACCCACG BSSSI	
251	ACGAGTGGGT TGCTCACCCA BssSI	TACATCGAAC ATGTAGCTTG	TGGATCTCAA ACCTAGAGTT	CAGCGGTAAG GTCGCCATTC	ATCCTTGAGA TAGGAACTCT	

Figure 28: functional map and sequence of pMCS cloning vector (continued)

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301	GTTTTCGCCC CAAAAGCGGG	CGAAGAACGT GCTTCTTGCA	TTTCCAATGA AAAGGTTACT	TGAGCACTTT ACTCGTGAAA	TAAAGTTCTG
351	CTATGTGGCG GATACACCGC	CGGTATTATC GCCATAATAG	CCGTATTGAC GGCATAACTG	GCCGGGCAAG CGGCCCGTTC	AGCAACTCGG TCGTTGAGCC
401	TCGCCGCATA AGCGGCGTAT	CACTATTCTC GTGATAAGAG	AGAATGACTT TCTTACTGAA	GGTTGAGTAC	TCACCAGTCA AGTGGTCAGT
451	CAGAAAAGCA GTCTTTTCGT	TCTTACGGAT AGAATGCCTA	GGCATGACAG CCGTACTGTC	TAAGAGAATT ATTCTCTTAA	ATGCAGTGCT TACGTCACGA
501	GCCATAACCA CGGTATTGGT	TGAGTGATAA ACTCACTATT	CACTGCGGCC	AACTTACTTC TTGAATGAAG	TGACAACGAT ACTGTTGCTA
551	CGGAGGACCG GCCTCCTGGC	AAGGAGCTAA TTCCTCGATT	CCGCTTTTTT GGCGAAAAAA	GCACAACATG CGTGTTGTAC	GGGGATCATG CCCCTAGTAC
601	TAACTCGCCT ATTGAGCGGA	TGATCGTTGG ACTAGCAACC	GAACCGGAGC CTTGGCCTCG	TGAATGAAGC ACTTACTTCG	CATACCAAAC GTATGGTTTG
651	GACGAGCGTG	ACACCACGAT	ACACCACGAT GCCTGTAGCA ATGGCAACAA CGTTCCCAA	ATGGGAACAA	なないだけが出出され

CTGCTCGCAC TGTGGTGCTA CGGACATCGT TACCGTTGTT GCAACGCGTT Figure 28: functional map and sequence of pMCS cloning vector (continued)

AseI	~~~~~~ CAATTAATAG GTTAATTATC	CTCGGCCCTT GAGCCGGGAA	AGCGTGGGTC TCGCACCCAG	TCCCGTATCG AGGGCATAGC	ACGAAATAGA TGCTTTATCT	AACTGTCAGA TTGACAGTCT	CATTTTAAT
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	TTCCCGGCAA	CACTTCTGCG	GGAGCCGGTG CCTCGGCCAC	TGGTAAGCCC	CTATGGATGA CATACCTACT	AAGCATTGGT	TTTAAAACTT
	TTACTCTAGC	GTTGCAGGAC	TGATAAATCT ACTATTTAGA	TGGGGCCAGA	AGTCAGGCAA TCAGTCCGTT	CTCACTGATT GAGTGACTAA	TTTAGATTGA
	GGCGAACTAC CCGCTTGATG	GGCGGATAAA CCGCCTATTT	GGTTTATTGC CCAAATAACG	ATTGCAGCAC TAACGTCGTG	CACGACGGGG GTGCTGCCCC	AGATAGGTGC TCTATCCACG	TCATATATAC
	ACTATTAACT TGATAATTGA	ACTGGATGGA TGACCTACCT	CCGGCTGGCT	TCGCGGTATC AGCGCCATAG	TAGTTATCTA ATCAATAGAT	CAGATCGCTG GTCTAGCGAC	CCAAGTTTAC
	701	751	801	851	901	951	1001

Figure 28: functional map and sequence of pMCS cloning vector (continued)

1051	TTAAAAGGAT AATTTTCCTA	CTAGGTGAAG GATCCACTTC	ATCCTTTTTG TAGGAAAAAC	ATAATCTCAT TATTAGAGTA	GACCAAAATC CTGGTTTTAG
1101	CCTTAACGTG GGAATTGCAC	AGTTTTCGTT TCAAAAGCAA	CCACTGAGCG GGTGACTCGC	TCAGACCCCG	TAGAAAAGAT ATCTTTTCTA
1151	CAAAGGATCT GTTTCCTAGA	TCTTGAGATC AGAACTCTAG	CTTTTTTTCT GAAAAAAAGA	GCGCGTAATC CGCGCATTAG	TGCTGCTTGC ACGACGAACG
1201	AAACAAAAAA TTTGTTTTTT	ACCACCGCTA	CCAGCGGTGG	TTTGTTTGCC AAACAAACGG	GGATCAAGAG CCTAGTTCTC
1251	CTACCAACTC GATGGTTGAG	TTTTTCCGAA AAAAAGGCTT	GGTAACTGGC CCATTGACCG Eo	C TTCAGCAGAG G AAGTCGTCTC Eco57I	CGCAGATACC GCGTCTATGG
,					
1301	AAATACTGIC TTTATGACAG	CTTCTAGTGT GAAGATCACA	AGCCGTAGTT TCGGCATCAA	AGGCCACCAC TCCGGTGGTG	T'TCAAGAACT AAGTTCTTGA
1351	CTGTAGCACC GACATCGTGG	GCCTACATAC CGGATGTATG	CTCGCTCTGC	TAATCCTGTT ATTAGGACAA	ACCAGTGGCT TGGTCACCGA

TGCTGGCCTT

AAACGCCAGC AACGCGGCCT TTTTACGGTT CCTGGCCTTT

1751

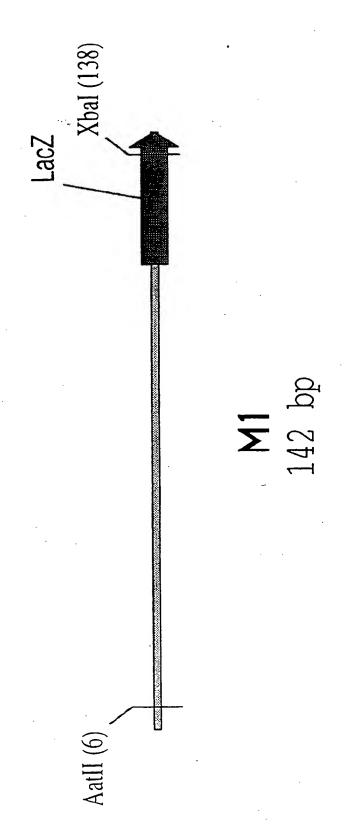
Figure 28: functional map and sequence of pMCS cloning vector (continued)

CAAGACGATA GTTCTGCTAT	TCGTGCACAC	CCTACAGCGT GGATGTCGCA	CGGACAGGTA	GAGCTTCCAG CTCGAAGGTC	CCACCTCTGA	GCCTATGGAA
GGGTTGGACT CCCAACCTGA	AACGGGGGGT TTGCCCCCCA	AACTGAGATA TTGACTCTAT	GGGAGAAAGG CCCTCTTTCC	GCGCACGAGG CGCGTGCTCC BSSSI	TCGGGTTTCG AGCCCAAAGC	GGGGGGCGGA
GTGTCTTACC CACAGAATGG	GGTCGGGCTG CCAGCCCGAC	ACCTACACCG TGGATGTGGC	GCTTCCCGAA CGAAGGGCTT	GAACAGGAGA CTTGTCCTCT	TATAGTCCTG ATATCAGGAC	ATGCTCGTCA TACGAGCAGT
GCGATAAGTC CGCTATTCAG	AAGGCGCAGC TTCCGCGTCG	GGAGCGAACG CCTCGCTTGC	AAAGCGC AC GCTTCCCGAA TTTCGCGGTG CGAAGGGCTT	GGCAGGGTCG GAACAGGAGA CCGTCCCAGC CTTGTCCTCT	CTGGTATCTT GACCATAGAA	GATTTTTGTG CTAAAAACAC
GCTGCCAGTG CGACGGTCAC	GTTACCGGAT CAATGGCCTA	AGCCCAGCTT TCGGGTCGAA	GAGCTATGAG CTCGATACTC	TCCGGTAAGC AGGCCATTCG	GGGGAAACGC	CTTGAGCGTC GAACTCGCAG
1401	1451	1501	1551	1601	1651	1701
			CUDETE	**************************************	73723	

AACCOURARA ACCOUNTABLE SOUNDSCHIE Figure 28: functional map and sequence of pMCS cloning vector (continued)

		-A C.		7)		
ACGACCGGAA	BsrGI	CCCCCCTGTA	AatII	CCCCGACGTC GGGGCTGCAG	ECORI	TTCACGT AAGTGCA
GGACCGGAAA	PacI	AATTAACCCC TTAATTGGGG	BglII	CCCCCCCAG ATCTCCCCCC GGGGGGGTC TAGAGGGGGG	ECORI	CCCCCCGAA TTCACGT GGGGGGCTT AAGTGCA
TTGCGCCGGA AAAATGCCAA GGACCGGAAA ACGACCGGAA	}	CCCCCCCTT AATTAACCCCCGGGGGGGGGGGGGGGGGGG	δg	CCCCCCCAG	Sphi	ACCCCCCCC CGCATGCCCC TGGGGGGGG GCGTACGGGG
TTGCGCCGGA	HindIII	GTAAGCTTCC CATTCGAAGG	NheI	CCGCTAGCCC	?	ACCCCCCCCC TGGGGGGGGG
57,1.957,51,1.1		TTGCTCACAT AACGAGTGTA	BsrGI	CACCCCCCCC	XbaI	CCCCCTCTAG
		1801		1851		1901
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Figure 29: functional map and sequence of pCAL module M1



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TGTGAGTTAG CTCACTCATT AGGCACCCCA GGCTTTACAC	ACACTCAATC GAGTGAGTAA TCCGTGGGGT CCGAAATGTG
AGGCACCCCA	TCCGTGGGGT
CTCACTCATT	GAGTGAGTAA
TGTGAGTTAG	ACACTCAATC
GACGTCTTAA	CTGCAGAATT
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GATAACAATT CTATTGTTAA TAACACTCGC ATTGTGAGCG GTTGTGTGGA CAACACACCT GCCGAGCATA CGGCTCGTAT AAATACGAAG TTTATGCTTC 51

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Figure 30: functional map and sequence of pCAL module M7-II

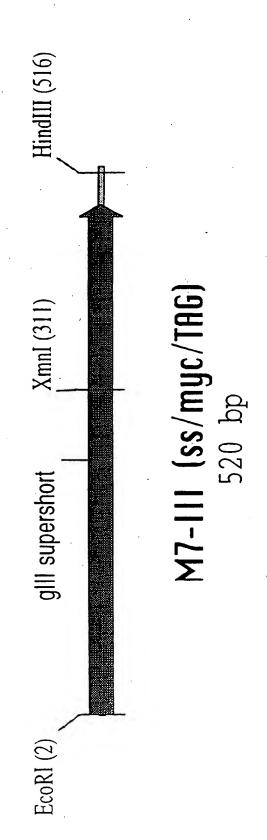


Figure 30: functional map and sequence of pCAL module M7-II (continued)

		GTGGTGGCTC	CACCACCGAG
		CTCTGAGGAG GATCTGTAGG GTGGTGGCTC	GAGACTCCTC CTAGACATCC CACCACCGAG
		CTCTGAGGAG	GAGACTCCTC
		AGAAGCTGAT	TCTTCGACTA
なこのなり	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	GAATTCGAGC	CTTAAGCTCG
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•		•			
A TACTITICTA CCGTTTGCGA TTATTCCCCC	CCGTTTGCGA	TACTTTTCTA	CTAAAACTAA	ACCAAGGCCA	
GAITITICAL AIGHAAGAI GGCAAACGCI AAIAAGGGGG	GGCAAACGCI	ATGAAAAGAT	GAT"I"I"I"I"I		75

CGCTAAAGGC	GCGATTTCCG	
AAATGCCGAT GAAAACGCGC TACAGTCTGA CGCTAAAGGC	TTTACGGCTA CTTTTGCGCG ATGTCAGACT GCGATTTCCG	
GAAAACGCGC	CTTTTGCGCG	
AAATGCCGAT	TTTACGGCTA	
CTATGACCGA	GATACTGGCT	
101		

ATGGTTTCAT	TACCAAAGTA	GGTGATTTTG
GCTGCTATCG ATGGTTTCAT	ACTAATGCCA CGACGATAGC	TCCGGCCTTG CTAATGGTAA TGGTGCTACT GGTGATTTTG
CTGTCGCTAC TGATTACGGT	ACTAATGCCA	CTAATGGTAA
CTGTCGCTAC	GACAGCGATG	TCCGGCCTTG
AAACTTGATT	TTTGAACTAA	TGGTGACGTT
151		201

CCACTAAAAC	TAATTCACCT ATTAAGTGGA
AGGCCGGAAC GATTACCATT ACCACGATGA CCACTAAAAC	TTCCCAAATG GCTCAAGTCG GTGACGGTGA TAATTCACCT AAGGGTTTAC CGAGTTCAGC CACTGCCACT ATTAAGTGGA
GATTACCATT	GCTCAAGTCG CGAGTTCAGC
AGGCCGGAAC	TTCCCAAATG AAGGGTTTAC
ACCACTGCAA	CTGGCTCTAA GACCGAGATT
4 > 0	251

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TTAGCCAACT AATCGGTTGA TCCCTCCTC AGGGAGGGAG ATATTTACCT TATAAATGGA ATTTCCGTCA TAAAGGCAGT AATTACTTAT TTAATGAATA 301

Figure 30: functional map and sequence of pCAL module M7-II (continued)

TCTTTTATATA	TCTTTGCGTT AGAAACGCAA	TTCCGTGGTG AAGGCACCAC	AATAAACTTA TTATTTGAAT	ATTGTGACAA TAACACTGTT	401
TTTTCTATTG AAAAGATAAC	GCGCTGGTAA ACCATATGAA TTTTCTATTG CGCGACCATT TGGTATACTT AAAAGATAAC	GCGCTGGTAA ACCATATGAA TTTTTCTATTG CGCGACCATT TGGTATACTT AAAAGATAAC	TTTGTCTTTG AAACAGAAAC	ATGTCGCCCT TACAGCGGGA	351

TACTGCGTAA

TTTGCTAACA

ATTTTCTACG

TTATGTATGT

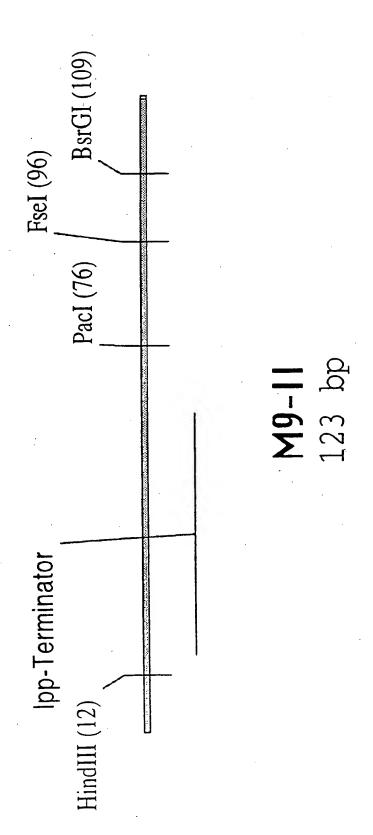
GTTGCCACCT

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HindIII	
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501 TAAGGAGTCT TGATAAGCTT ATTCCTCAGA ACTATTCGAA

Figure 31: functional map and sequence of pCAL module M9-II



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AGATTGTGCG TCTAACACGC AAAATGGCGC TTTTACCGCG TGTGAAGTGA ACACTTCACT AAGCTTGACC TTCGAACTGG 9999999999

FseI PacI

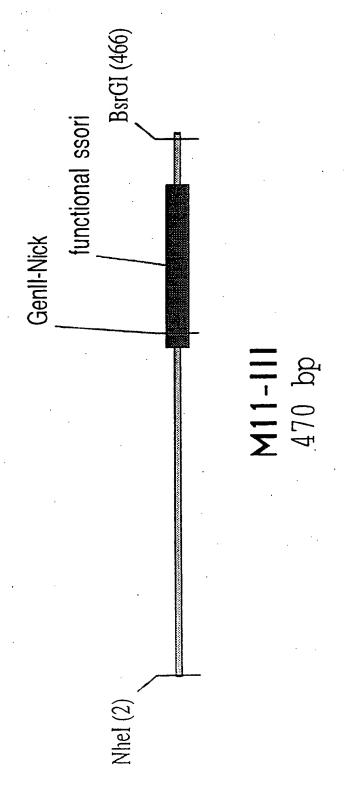
GCCGGCCTGG CGGCCGGACC 9999999999 TTAATTAAAG TGTCTGCCGT ACAGACGGCA ACATTTTTT TGTAAAAAA 51

GGGCCC ACAGGGGGG GGGGGGTGT 101

BsrGI

TGTCCCCCC CCCCCCACA

Figure 32: functional map and sequence of pCAL module M11-III



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Figure 32: functional map and sequence of pCAL module M11-III (continued)

	NheI				
ᆏ	GCTAGCACGC	GCCCTGTAGC CGGGACATCG	GGCGCATTAA CCGCGTAATT	ວວວອວວອວອວ	TGTGGTGGTT ACACCACCAA
51	ACGCGCAGCG TGCGCGTCGC	TGACCGCTAC ACTGGCGATG	ACTTGCCAGC TGAACGGTCG	GCCCTAGCGC CGGGATCGCG	CCGCTCCTTT
101	CGCTTTCTTC GCGAAAGAAG	CCTTCCTTTC GGAAGGAAAG	TCGCCACGTT AGCGGTGCAA	CGCCGGCTTT GCGGCCGAAA	CCCCGTCAAG GGGGCAGTTC
151	CTCTAAATCG GAGATTTAGC	GGGCATCCCT CCCGTAGGGA	TTAGGGTTCC AATCCCAAGG	GATTTAGTGC CTAAATCACG	TTTACGGCAC AAATGCCGTG
201	CTCGACCCCA GAGCTGGGGT	AAAAACTTGA TTTTT®AACT	TTAGGGTGAT AATCCCACTA	GGTTCTCGTA CCAAGAGCAT	GTGGGCCATC CACCCGGTAG
251	GCCCTGATAG	ACGGTTTTTTC TGCCAAAAAG	GCCCTTTGAC	GTTGGAGTCC CAACCTCAGG	ACGTTCTTTA TGCAAGAAAT
301	ATAGTGGACT TATCACCTGA	CTTGTTCCAA GAACAAGGTT	ACTGGAACAA TGACCTTGTT	CACTCAACCC GTGAGTTGGG	TATCTCGGTC ATAGAGCCAG
351	TATTCTTTTG	ATTTATAAGG	ATTTATAAGG GATTTTGCCG ATTTCGGCCT ATTGGTTAAA	ATTTCCCCT	ע ע ע שיייטטיייי ע

	TAAATATTCC CTAAAACGGC TAAAGCCGGA TAACCAATTT
(continued)	CTAAAACGGC
of pCAL module M11-III (continued	TAAATATTCC C
Figure 32: functional map and sequence	ATAAGAAAAC

AAAATATTAA TTTATATT GAATTTTAAC CTTAAAATTG AATTTAACGC TTAAATTGCG ATTTAACAAA AAATGAGCTG 401

TAAATTGTTT TTTACTCGAC

BsrGI ~ ~ ~ ~ ~ ~

AAGTACATGT TTCATGTACA CGTTTACAAT GCAAATGTTA

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Figure 33; functional map and sequence of pCAL module M14-Ext2

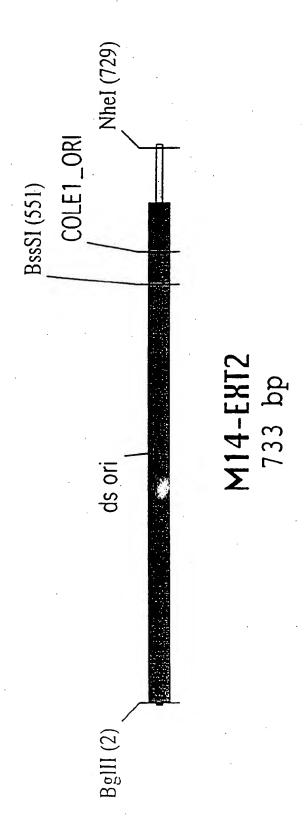


Figure 33: functional map and sequence of pCAL module M14-Ext2 (continued)

.	Bglii				
~	AGATCTGACC TCTAGACTGG	AAAATCCCTT TTTTAGGGAA	AACGTGAGTT TTGCACTCAA	TTCGTTCCAC	TGAGCGTCAG ACTCGCAGTC
51	ACCCCGTAGA TGGGGCATCT	AAAGATCAAA TTTCTAGTTT	GGATCTTCTT CCTAGAAGAA	GAGATCCTTT CTCTAGGAAA	TTTTCTGCGC AAAAGACGCG
101	GTAATCTGCT CATTAGACGA	GCTTGCAAAC CGAACGTTTG	AAAAAAACCA TTTTTTGGT	CCGCTACCAG GGCGATGGTC	CGGTGGTTTG GCCACCAAAC
151	TTTGCCGGAT AAACGGCCTA	CAAGAGCTAC GTTCTCGATG	CAACTCTTTT GTTGAGAAAA	TCCGAAGGTA AGGCTTCCAT	ACTGGCTACA
201	GCAGAGCGCA CGTCTCGCGT	GATACCAAAT CTATGGTTTA	ACTGTTCTTC TGACAAGAAG	TAGTGTAGCC ATCACATCGG	GTAGTTAGGC CATCAATCCG
251	CACCACTTCA GTGGTGAAGT	AGAACTCTGT TCTTGAGACA	AGCACCGCCT TCGTGGCGGA	ACATACCTCG TGTATGGAGC	CTCTGCTAAT
301	CCTGTTACCA	GTGGCTGCTG	CCAGTGGCGA GGTCACCGCT	TAAGTCGTGT ATTCAGCACA	CTTACCGGGT GAATGGCCCA
351	TGGACTCAAG	ACGATAGTTA	CCGGATAAGG	CGCAGCGGTC	GGGCTGAACG

ure 33: fi	Figure 33: functional map and sequene ACCTGAGTTC	ince of pCAL module M14-Ext2 (continued) CTGCTATCAAT GGCCTA	xt2 (continued) GGCCTATTCC	GCGTCGCCAG	CCCGACTTGC
401	GGGGGTTCGT	GCACACAGCC	CAGCTTGGAG	CGAACGACCT	ACACCGAACT
	CCCCCAAGCA	CGTGTGTCGG	GTCGAACCTC	GCTTGCTGGA	TGTGGCTTGA
451	GAGATACCTA	CAGCGTGAGC	TATGAGAAAG	CGCCACGCTT	CCCGAAGGGA
	CTCTATGGAT	GTCGCACTCG	ATACTCTTTC	GCGGTGCGAA	GGGCTTCCCT
501	GAAAGGCGGA CTTTCCGCCT	CAGGTATCCG GTCCATAGGC	GTAAGCGGCA CATTCGCCGT	GGGTCGGAAC CCCAGCCTTG	AGGAGAGCGC TCCTCTCGCG BSSSI
551	ACGAGGGAGC TGCTCCCTCG BSSSI	TTCCAGGGGG AAGGTCCCCC	AAACGCCTGG TTTGCGGACC	TATCTTTATA ATAGAAATAT	GTCCTGTCGG CAGGACAGCC
601	GTTTCGCCAC	CTCTGACTTG	AGCGTCGATT	TTTGTGATGC	TCGTCAGGGG
	CAAAGCGGTG	GAGACTGAAC	TCGCAGCTAA	AAACACTACG	AGCAGTCCCC
651	GGCGGAGCCT	ATGGAAAAAC	GCCAGCAACG	CGGCCTTTTT	ACGGTTCCTG
	CCGCCTCGGA	TACCTTTTTG	CGGTCGTTGC	GCCGGAAAAA	TGCCAAGGAC

Figure 33: functional map and sequence of pCAL module M14-Ext2 (continued)

NheI

GGCCTTTTGC TCACATGGCT AGC CCGGAAAACG AGTGTACCGA TCG GGCCTTTTGC GCCTTTTGCT CGGAAAACGA 701

Figure 34: functional map and sequence of pCAL module M17

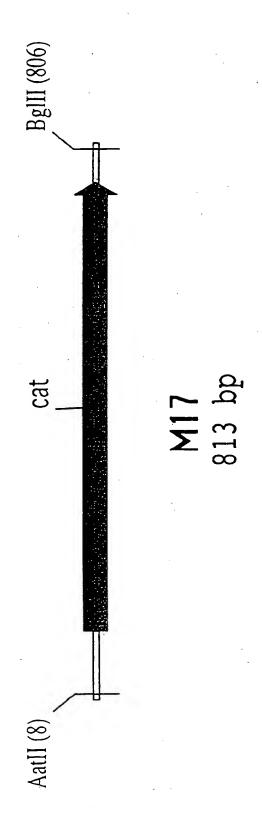


Figure 34: functional map and sequence of pCAL module M17 (continued)

AatII

\vdash	GGGACGTCGG	GTGAGGTTCC CACTCCAAGG	AACTTTCACC TTGAAAGTGG	ATAATGAAAT TATTACTTTA	AAGATCACTA TTCTAGTGAT	
51	CCGGGCGTAT	TTTTTGAGTT AAAAACTCAA	ATCGAGATTT TAGCTCTAAA	TCAGGAGCTA AGTCCTCGAT	AGGAAGCTAA TCCTTCGATT	
101	AATGGAGAAA TTACCTCTTT	AAAATCACTG TTTTAGTGAC	GATATACCAC CTATATGGTG	CGTTGATATA GCAACTATAT	TCCCAATGGC AGGGTTACCG	
151	ATCGTAAAGA TAGCATTTCT	ACATTTTGAG TGTAAAACTC	GCATTTCAGT CGTAAAGTCA	CAGTTGCTCA GTCAACGAGT	ATGTACCTAT TACATGGATA	
201	AACCAGACCG TTGGTCTGGC	TTCAGCTGGA AAGTCGACCT	TATTACGGCC	TTTTTAAAGA AAAAATTTCT	CCGTAAAGAA GGCATTTCTT	
251	AAATAAGCAC TTTATTCGTG	AAGTTTTATC TTCAAAATAG	CGGCCTTTAT GCCGGAAATA	TCACATTCTT AGTGTAAGAA	GCCCGCCTGA CGGGCGGACT	
301	TGAATGCTCA ACTTACGAGT	CCCGGAGTTC GGGCCTCAAG	CGTATGGCAA GCATACCGTT	TGAAAGACGG ACTTTCTGCC	TGAGCTGGTG ACTCGACCAC	
351	ATATGGGATA	GTGTTCACCC	TTGTTACACC	GTTTTCCATG	AGCAAACTGA	

AAACGCCTGG

GGGTGCCCTT

GGCAGTTATT

ATTTTTAA

GCGGGGCGTA

751

GAGTGGCAGG

GTACTGCGAT

AATTACAACA

ATGCTTAATG

TACGAATTAC

ACAGCCGTCT

TGTCGGCAGA

701

TTAATGTTGT

CATGACGCTA

CTCACCGTCC

Figure 34: functional map and sequence of pCAL module M17 (continued)

CGGCAGTTTC GCCGTCAAAG CCAATCCCTG CGACAAGGTG GCTGTTCCAC ATGGCTTCCA TCGTTTGACT CCTGGCCTAT GGACCGGATA GGTTAGGGAC CTGTTGAAGA TACCGAAGGT GACAACTTCT CAAAAGGTAC AGCCAATATG ATACGCAAGG GCCGTTTGTG CGACGATTTC GCTGCTAAAG TGCCACTTTT TTCGTCTCAG TCGGTTATAC TATGCGTTCC CGGCAAACAC ACGGTGAAAA AAGCAGAGTC AACAATGTGG ATTTAAACGT GGCAAATATT GTGAATACCA GAATATGTTT CTTATACAAA TAAATTTGCA GGTTCATCAT CCAAGTAGTA GTGGCGTGTT CACCGCACAA CACTTATGGT CCGTTTATAA CACAAGTGGG TGGCGATTCA TCGCTCTGGA GGTTTATTGA TTTCACTATG AAGCGTTCTA CCAAATAACT ACCAGTTTTG TGGTCAAAAC AAAGTGATAC ACCGCTAAGT AGCGAGACCT TTCGCAAGAT TATACCCTAT AGCGGGGGCA TTGCAAAAGT CCACTCAAAG GACTACGGCG ATGTGTATAT TTCCCTAAAG AAGGGATTTC CTGATGCCGC AACGTTTTCA TACACATATA TCGCCCCCGT GGTGAGTTTC 501 451 551 401 601 651

Figure 34; functional map and sequence of pCAL module M17 (continued)

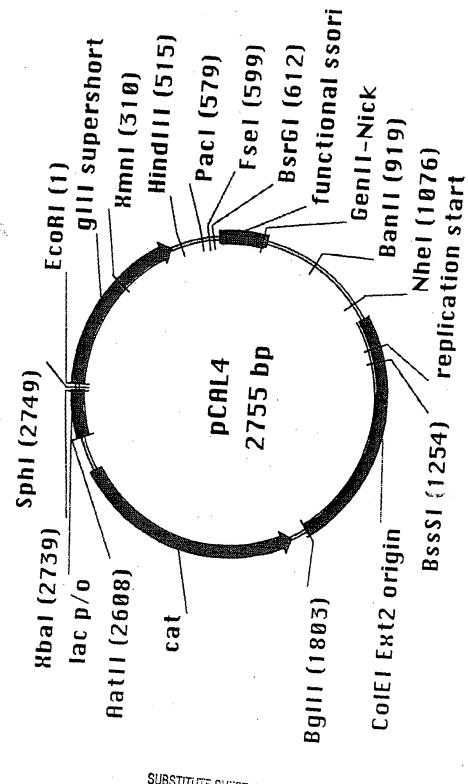
TAAAAAATT CCGTCAATAA CCCACGGGAA TTTGCGGACC CGCCCCGCAT

BglII

801 TGCTAGATCT I

I TGCTAGATCT TO

Figure 35: functional map and sequence of modular vector pCAL4



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Figure 35: functional map and sequence of modular vector pCAL4 (continued)

	EcoRI				
	? ? ? ? ? ?				
\leftarrow	AATTCGAGCA	GAAGCTGATC	TCTGAGGAGG	ATCTGTAGGG	TGGTGGCTCT
	TTAAGCTCGT	CTTCGACTAG	AGACTCCTCC	CTTCGACTAG AGACTCCTCC TAGACATCCC ACCACCGAGA	ACCACCGAGA

ATAAGGGGGC	TATTCCCCCG	GCTAAAGGCA
ATTITIGATIA IGAAAAGAIG GCAAACGCIA ATAAGGGGGC	CGTTTGCGAT	AATGCCGATG AAAACGCGCT ACAGTCTGAC
TGAAAAGATG	TAAAACTAAT ACTTTTCTAC	AAAACGCGCT
ATTTTGATTA	TAAAACTAAT	AATGCCGATG
GGTTCCGGTG	CCAAGGCCAC	TATGACCGAA
51		101

 -					
 151	AACTTGATTC	TGTCGCTACT	TGTCGCTACT GATTACGGTG CTGCTATCGA TGGTTTCATT	CTGCTATCGA	TGGTTTCATT
	TTGAACTAAG	ACAGCGATGA	CTAATGCCAC	GACGATAGCT	ACAGCGATGA CTAATGCCAC GACGATAGCT ACCAAAGTAA

GTGATTTTGC	GGCCGGAACG ATTACCATTA CCACGATGAC CACTAAAACG
T CCGGCCTTGC TAATGGTAAT GGTGCTACTG GTGATTTTGC	CCACGATGAC
TAATGGTAAT	ATTACCATTA
CCGGCCTTGC	GGCCGGAACG
GGTGACGTTT	CCACTGCAAA
201	

AATTCACCTT	TTAAGTGGAA
NAT TCCCAAATGG CTCAAGTCGG TGACGGTGAT AATTCACCTT	TA AGGGTTTACC GAGTTCAGCC ACTGCCACTA TTAAGTGGAA
CTCAAGTCGG	GAGTTCAGCC
TCCCAAATGG	AGGGTTTACC
TGGCTCTAAT	ACCGAGATTA
251	

XmnI

ATCGGTTGAA	AAAGGCAGTT ATAAATGGAA GGGAGGGAGT TAGCCAACTT
A TITCCGICAA TAITIACCII CCCICCCICA AICGGIIGAA	GGGAGGGAGT
TATTTACCTT	ATAAATGGAA
TTTCCGTCAA	IT AAAGGCAGTT ATAAATG
TAATGAATAA	ATTACTTATT
301	

Figure 35: functional map and sequence of modular vector pCAL4 (continued)

351	TGTCGCCCTT ACAGCGGGAA	TTGTCTTTGG AACAGAAACC	CGCTGGTAAA GCGACCATTT	CCATATGAAT GGTATACTTA	TTTCTATTGA AAAGATAACT
	TTGTGACAAA AACACTGTTT	ATAAACTTAT TATTTGAATA	TCCGTGGTGT AGGCACCACA	CTTTGCGTTT GAAACGCAAA	CTTTTATATG GAAAATATAC
451	TTGCCACCTT AACGGTGGAA	TATGTATGTA ATACATACAT	TTTTCTACGT AAAAGATGCA	TTGCTAACAT	ACTGCGTAAT TGACGCATTA
501	AAGGAGTCTT TTCCTCAGAA	HindIII ~~~~~ GATAAGCTTG CTATTCGAAC	ACCTGTGAAG TGGACACTTC	TGAAAAATGG ACTTTTTACC	CGCAGATTGT GCGTCTAACA
		v. 	PacI		FSEI
551	GCGACATTTT CGCTGTAAAA	TTTTGTCTGC AAAACAGACG	CGTTTAATTA GCAAATTAAT	AAGGGGGGGG	9900990000
		BsrGI			
601	TGGGGGGGGG	TGTACATGAA ACATGTACTT	ATTGTAAACG TAACATTTGC	ТТААТАТТТТ ААТТАТАААА	GTTAAAATTC CAATTTTAAG

Figure 35: functional map and sequence of modular vector pCAL4 (continued)

651	GCGTTAAATT CGCAATTTAA	TTTGTTAAAT AAACAATTTA	CAGCTCATTT GTCGAGTAAA	TTTAACCAAT AAATTGGTTA	AGGCCGAAAT TCCGGCTTTA	
701	CGGCAAAATC GCCGTTTTAG	CCTTATAAAT GGAATATTTA	CAAAAGAATA GTTTTCTTAT	GACCGAGATA CTGGCTCTAT	GGGTTGAGTG CCCAACTCAC	•
751	TTGTTCCAGT AACAAGGTCA	TTGGAACAAG	AGTCCACTAT TCAGGTGATA	TAAAGAACGT ATTTCTTGCA	GGACTCCAAC CCTGAGGTTG	•
801	GTCAAAGGGC	GAAAAACCGT CTTTTTGCA	CTATCAGGGC GATAGTCCCG	GATGGCCCAC CTACCGGGTG	TACGAGAACC ATGCTCTTGG	
851	ATCACCCTAA TAGTGGGATT	TCAAGTTTTT AGTTCAAAAA	TGGGGTCGAG ACCCCAGCTC	GTGCCGTAAA CACGGCATTT	GCACTAAATC CGTGATTTAG	
		BanII				
901	GGAACCCTAA CCTTGGGATT	AGGGAGCCCC TCCCTCGGGG	CGATTTAGAG GCTAAATCTC	CTTGACGGGG GAACTGCCCC	AAAGCCGGCG TTTCGGCCGC	
951	AACGTGGCGA TTGCACCGCT	GAAAGGAAGG	GAAGAAAGCG	AAAGGAGCGG TTTCCTCGCC	GCGCTAGGGC	

			•			
9292992999 2929229222	AAAGGCCAGC TTTCCGGTCG	TTTCCATAGG AAAGGTATCC	GTCAGAGGTG CAGTCTCCAC	CCTGGAAGCT GGACCTTCGA	ATACCTGTCC TATGGACAGG	CACGCTGTAG
AACCACCACA TTGGTGGTGT	CATGTGAGCA GTACACTCGT	TGCTGGCGTT ACGACCGCAA	CGACGCTCAA GCTGCGAGTT	GGCGTTTCCC CCGCAAAGGG	CGCTTACCGG	TCTCATAGCT AGAGTATCGA
GCGT	NheI ~~~~~~ GCGTGCTAGC CGCACGATCG	AAGGCCGCGT TTCCGGCGCA	TCACAAAAAT AGTGTTTTTA	AAAGATACCA TTTCTATGGT	CCGACCCTGC	CGTGGCGCTT
GTAGCGGTCA CGCTGC	GCTACAGGGC	GAACCGTAAA CTTGGCATTT	CTGACGAGCA GACTGCTCGT	ACAGGACTAT TGTCCTGATA	CTCTCCTGTT GAGAGGACAA	CTTCGGGAAG GAAGCCCTTC
Figure 35: functional map and sequence 1001 GCTGGCAAGT C	TTAATGCGCC	AAAAGGCCAG TTTTCCGGTC	CTCCGCCCCC	GCGAAACCCG CGCTTTGGGC	BSSSI ~~~~~ CCTCGTGCG GGGAGCACGC	GCCTTTCTCC
Figure 35: ful 1001	1051	1101	1151	1201	1251	1301

Figure 35: functional map and sequence of modular vector pCAL4 (continued)

	1351	GTATCTCAGT CATAGAGTCA	TCGGTGTAGG AGCCACATCC	TCGTTCGCTC AGCAAGCGAG	CAAGCTGGGC GTTCGACCCG	TGTGTGCACG ACACACGTGC
	1401	AACCCCCCGT TTGGGGGGCA	TCAGCCCGAC AGTCGGGCTG	CGCTGCGCCT GCGACGCGGA	TATCCGGTAA ATAGGCCATT	CTATCGTCTT GATAGCAGAA
_	1451	GAGTCCAACC	CGGTAAGACA GCCATTCTGT	CGACTTATCG GCTGAATAGC	CCACTGGCAG GGTGACCGTC	CAGCCACTGG GTCGGTGACC
	1501	TAACAGGATT ATTGTCCTAA	AGCAGAGCGA TCGTCTCGCT	GGTATGTAGG CCATACATCC	CGGTGCTACA GCCACGATGT	GAGTTCTTGA
OUEEE (DIS	1551	AGTGGTGGCC TCACCACCGG	TAACTACGGC ATTGATGCCG	TACACTAGAA ATGTGATCTT	GAACAGTATT CTTGTCATAA	TGGTATCTGC ACCATAGACG
F Oc\	1601	GCTCTGCTGT CGAGACGACA	AGCCAGTTAC TCGGTCAATG	CTTCGGAAAA GAAGCCTTTT.	AGAGTTGGTA TCTCAACCAT	GCTCTTGATC CGAGAACTAG
	1651	CGGCAAACAA GCCGTTTGTT	ACCACCGCTG TGGTGGCGAC	GTAGCGGTGG CATCGCCACC	TTTTTTTGTT AAAAAAACAA	TGCAAGCAGC
•	1701	AGATTACGCG TCTAATGCGC	CAGAAAAAAA GTCTTTTTT	GGATCTCAAG CCTAGAGTTC	AAGATCCTTT TTCTAGGAAA	GATCTTTTCT CTAGAAAAGA

.4 (continued)
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5: functional
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		,	. •			
GGATTTTGGT	TTAAAAAAT	CATTAAGCAT	TGAATCGCCA	CATAGTGAAA	CAAAACTGGT	TCAATAAACC
CCTAAAACCA	AATTTTTTA	GTAATTCGTA	ACTTAGCGGT	GTATCACTTT	GTTTTGACCA	AGTTATTTGG
TCACGTTAAG	AATAACTGCC	TGTTGTAATT	ATGATGAACC	AATATTTGCC	ACGTTTAAAT	AAACATATTC
AGTGCAATTC	TTATTGACGG	ACAACATTAA	TACTACTTGG	TTATAAACGG	TGCAAATTTA	TTTGTATAAG
GAACGAAAAC	TAAGGGCACC	ATCGCAGTAC	CACAAACGGC	CCTTGCGTAT	CATATTGGCT	CTGAGACGAA
CTTGCTTTTG		TAGCGTCATG	GTGTTTGCCG	GGAACGCATA	GTATAACCGA	GACTCTGCTT
ACGCTCAGTG	ACCAGGCGTT	CCTGCCACTC	TGGAAGCCAT	CACCTTGTCG	AGAAGTTGTC	CAGGGATTGG
TGCGAGTCAC	TGGTCCGCAA	GGACGGTGAG	ACCTTCGGTA	GTGGAACAGC	TCTTCAACAG	
ACGGGGTCTG TGCCCCAGAC	BglII ~~~~~~ CAGATCTAGC GTCTAGATCG	TACGCCCCGC ATGCGGGGCG	TCTGCCGACA	GCGGCATCAG	ACGGGGGCGA TGCCCCCGCT	GAAACTCACC CTTTGAGTGG
1751	1801	1851	1901	1951	2001	2051

	ATC
	AACACGCCAC
s: functional map and sequence of modular vector pCAL4 (continued)	HER ARCACACA THE THE TOP TO THE ARCACACAC ATC.
35: functional m	E
Figure .	, ,

ATCTTGCGAA	TCCAGAGCGA	TCAGTTTGCT CATGGAAAAC GGTGTAACAA GGGTGAACAC
TAGAACGCTT	AGGTCTCGCT	AGTCAAACGA GTACCTTTTG CCACATTGTT CCCACTTGTG
AACACGCCAC	TGGTATTCAC	GGTGTAACAA
TTGTGCGGTG	ACCATAAGTG	CCACATTGTT
ATAGGCCAGG TTTTCACCGT AACACGCCAC ATCTTGCGAA	GAAACTGCCG GAAATCGTCG TGGTATTCAC TCCAGAGCGA	TCAGTTTGCT CATGGAAAAC GGTGTAACAA GGGTGAACAC
TATCCGGTCC AAAAGTGGCA TTGTGCGGTG TAGAACGCTT	CTTTGACGGC CTTTAGCAGC ACCATAAGTG AGGTCTCGCT	AGTCAAACGA GTACCTTTTG CCACATTGTT CCCACTTGTG
ATAGGCCAGG	GAAACTGCCG	TCAGTTTGCT
TATCCGGTCC	CTTTGACGGC	AGTCAAACGA
CTTTAGGGAA	TATATGTGTA	TGAAAACGTT
GAAATCCCTT	ATATACACAT	ACTTTTGCAA
2101	2151	2201

SAACTCCGGG CTTGAGGCCC	
A CCGTCTTTCA TTGCCATACG GAACTCCGGG	
A CCGTCTTTCA I GGCAGAAAGT	
CACCAGCTCA GTGGTCGAGT	
TATCCCATAT ATAGGGTATA	
2251	
SUBSTITU	

TCAGGCGGGC AAGAATGTGA ATAAAGGCCG GATAAAACTTT AGTCCGCCCG TTCTTACACT TATTTCCGGC CTATTTTGAA	TICTITACGG TCTTTAAAAA GGCCGTAATA TCCAGCTGAA
ATAAAGGCCG TATTTCCGGC	GGCCGTAATA TCCAGCTGAA
AAGAATGTGA TTCTTACACT	TCTTTAAAAA
TCAGGCGGGC AGTCCGCCCG	TTCTTTACGG
TGAGCATTCA	GTGCŤTATTT
2301	2351
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AGGTCGACTT

CCGGCATTAT

AGAAATTTTT

AAGAAATGCC

CACGAATAAA

CTCAAAATGT	GAGTTTTACA
STT ATAGGTACAT TGAGCAACTG ACTGAAATGC CTCAAAATGT	CAA TATCCATGTA ACTCGTTGAC TGACTTTACG GAGTTTTACA
TGAGCAACTG	ACTCGTTGAC
ATAGGTACAT	TATCCATGTA
CGGTCTGGTT	CAGAC
2401)

CAGTGATTTT	GTCACTAAAA
GTGGTATATC	CACCATATAG
TATATCAACG GTGGTATATC CAGTGATTTT	ATATAGTTGC CACCATATAG
GCCATTGGGA	CGGTAACCCT
TCTTTACGAT	AGAAATGCTA
2451	

AACTCAAAAA	GGAACCTCAC
TTGAGTTTTT	CCTTGGAGTG
TAGCTCCTGA AAATCTCGAT	ATTTCATTAT GGTGAAAGTT
ATCGAGGACT TTTAGAGCTA	TAAAGTAATA CCACTTTCAA
TAGCTCCTGA	ATTTCATTAT GGTGAAAGTT
ATCGAGGACT	TAAAGTAATA CCACTTTCAA
TTAGCTTCCT	TAGTGATCTT
AATCGAAGGA	ATCACTAGAA
TTTCTCCATT	ATACGCCCGG
AAAGAGGTAA	TATGCGGGCC
2501	2551

Figure 35: functional map and sequence of modular vector pCAL4 (continued)

	ATGTGAGTTA GCTCACTCAT TAGGCACCCC AGGCTTTACA	
	TAGGCACCCC	THE PROPERTY OF THE PROPERTY O
	GCTCACTCAT	
	ATGTGAGTTA	田木木び田じ木じ木田
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	CCGACGTCTA	E K C K C C E C C C
	2601	
		^

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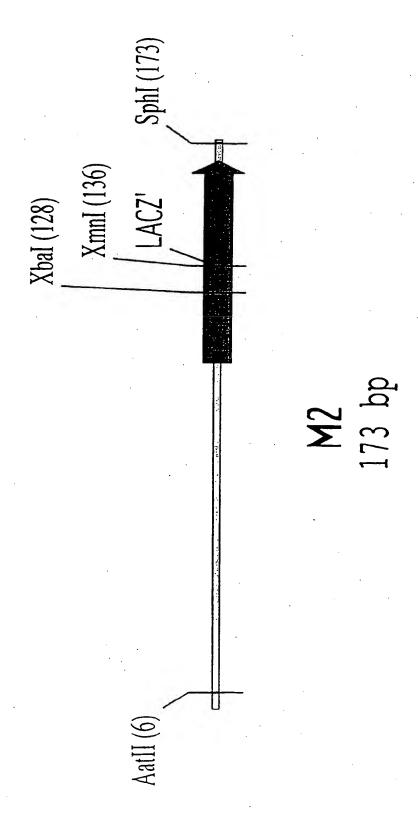
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	3G AAACAGCTAT GACCATGATT ACGAATTTCT AGAGCATGCG	C TTTGTCGATA CTGGTACTAA TGCTTAAAGA TCTCTTAACC
?	ACGAATTTCT	TGCTTAAAGA
	GACCATGATT	CTGGTACTAA
	AAACAGCTAT	TTTGTCGATA
	TTCACACAGG	AAGTGTGTCC
1		

SphI

XbaI

EcoRI

2751 GGGGG CCCCC



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GGCTTTACAC CCGAAATGTG AGGCACCCCA TCCGTGGGGT CTCACTCATT GAGTGAGTAA TGTGAGTTAG ACACTCAATC CTGCAGAATT GACGTCTTAA

GATAACAATT CTATTGTTAA ATTGTGAGCG TAACACTCGC GTTGTGTGGA CAACACACCT CGGCTCGTAT GCCGAGCATA AAATACGAAG TTTATGCTTC 51

XmnI

XbaI

CATATTACAT GTATAATGTA GAATAACTTC CTTATTGAAG ACCATGTCTA TGGTACAGAT AACAGCTATG TTGTCGATAC TCACACAGGA AGTGTGTCCT

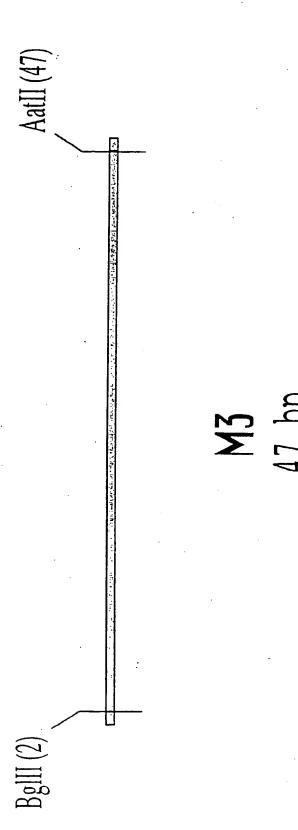
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 $\mathtt{TGC}$ AGTTATCGCA CGCTATACGA

51

ACG TCAATAGCGT GCGATATGCT

101

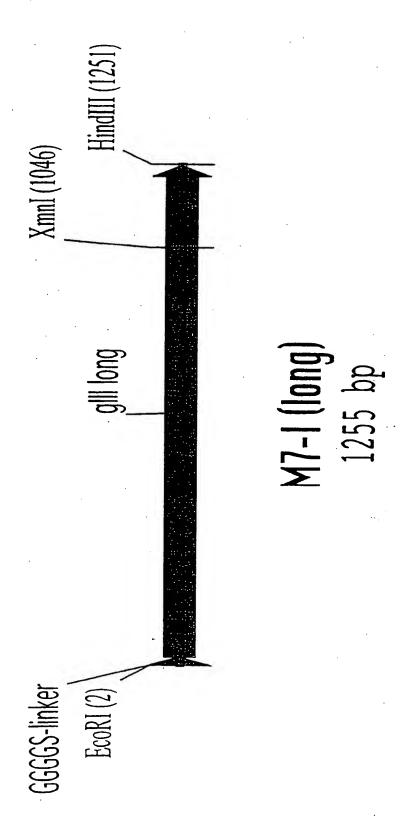


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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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TGACGTC ACTGCAG 11111 TACGAAGTTA ATGCTTCAAT ATGTATGCTA TACATACGAT ACTTCGTATA TGAAGCATAT AGATCTCATA TCTAGAGTAT



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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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Н	GAATTCGGTG	GTGGTGGATC	TGCGTGCGCT	GAAACGGTTG	AAAGTTGTTT
	CTTAÄGCCAC	CACCACCTAG	ACGCACGCGA	CTTTGCCAAC	TTTCAACAAA
51	AGCAAAATCC	CATACAGAAA	ATTCATTTAC	TAACGTCTGG	AAAGACGACA
	TCGTTTTÄGG	GTATGTCTTT	TAAGTAAATG	ATTGCAGACC	TTTCTGCTGT
101	AAACTTTAGA	TCGTTACGCT	AACTATGAGG	GCTGTCTGTG	GAATGCTACA
	TTTGAAATCT	AGCAATGCGA	TTGATACTCC	CGACAGACAC	CTTACGATGT
151	GGCGTTGTAG	TTTGTACTGG AAACATGACC	TGACGAAACT ACTGCTTTGA	CAGTGTTACG GTCACAATGC	GTACATGGGT CATGTACCCA
201	TCCTATTGGG	CTTGCTATCC	CTGAAAATGA	GGGTGGTGGC	TCTGAGGGTG
	AGGATAACCC	GAACGATAGG	GACTTTTACT	CCCACCACCG	AGACTCCCAC
251	GCGGTTCTGA CGCCAAGACT	GGGTGGCGGT	TCTGAGGGTG AGACTCCCAC	GCGGTACTAA CGCCATGATT	ACCTCCTGAG TGGAGGACTC
301	TACGGTGATA	CACCTATTCC	GGGCTATACT	TATATCAACC	CTCTCGACGG
	ATGCCACTAT	GTGGATAAGG	CCCGATATGA	ATATAGTTGG	GAGAGCTGCC

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

CACTTATCCG GTGAATAGGC AACTCCTCAG CGAAATAGGC GCTTTATCCG CACTGACCCC	•	CCTGGTACTG GGACCATGAC TCAGCCTCTT AGTCGGAGAA AGGGGGCATT TCCCCCGTAA GTTAAAACTT	AGCAAAACCC TCGTTTTGGG AATACTTTCA TTATGAAAGT TTGACAAATA TTGACAAATA TTGACAGTA TTACCAGTA	CGCTAATCCT GCGATTAGGA TGTTTCAGAA ACAAAGTCTT ACGGGCACTG TGCCCGTGAC TGCCCGTGAC	AATCCTTCTC TTAGGAAGAG TAATAGGTTC ATTATCCAAGG AATGAGTTCC TCATCAAAAG
CCATGTATGA CGCTTACTGG GGTACATACT GCGAATGACC	•	rgg Acc	AACGGTAAAT TTGCCATTTA	TCAGAGACTG	CGCTTTCCAT GCGAAAGGTA
TCTGGCTTTA ATGAGGATTT AGACCGAAAT TACTCCTAAA	•	l'T'T AAA	ATTTGTTTGT TAAACAAACA	GAATATCAAG	GCCAATCGTC CGGTTAGCAG
TGACCTGCCT CAACCTCCTG ACTGGACGGA GTTGGAGGAC		CTG	TCAATGCTGG AGTTACGACC	CGGCGGCTCT GCCGCCGAGA	GGTGGTGGTT CCACCACCAA
CTGGTGGCGG CTCTGAGGGT GACCACCGCC GAGACTCCCA		GT	GGTGGCTCTG CCACCGAGAC	AGGGTGGCGG TCCCACCGCC	TTCTGAGGGT AAGACTCCCA

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

751	GGCGGCTCTG CCGCCGAGAC	AGGGAGGCGG TCCCTCCGCC	TTCCGGTGGT AAGGCCACCA	GGCTCTGGTT CCGAGACCAA	CCGGTGATTT GGCCACTAAA
801	TGATTATGAA ACTAATACTT	AAGATGGCAA TTCTACCGTT	ACGCTAATAA TGCGATTATT	GGGGGCTATG CCCCCGATAC	ACCGAAAATG TGGCTTTTAC
851	CCGATGAAAA GGCTACTTTT	CGCGCTSCAG	TCTGACGCTA AGACTGCGAT	AAGGCAAACT TTCCGTTTGA	TGATTCTGTC ACTAAGACAG
901	GCTACTGATT CGATGACTAA	ACGGTGCTGC TGCCACGACG	TATCGATGGT ATAGCTACCA	TTCATTGGTG AAGTAACCAC	ACGTTTCCGG TGCAAAGGCC
951	CCTTGCTAAT GGAACGATTA	GGTAATGGTG	CTACTGGTGA GATGACCACT	TTTTGCTGGC AAAACGACCG	TCTAATTCCC AGATTAAGGG
1001	AAATGGCTCA TTTACCGAGT	AGTCGGTGAA TCAGCCACTT	GGTGATAATT CCACTATTAA	CACCTTTAAT GTGGAAATTA	XmnI ~~~~~~~ GAATAATTTC CTTATTAAAG
1051	CGTCAATATT GCAGTTATAA	TACCTTCCAT ATGGAAGGTA	CCCTCAATCG	GTTGAATGTC CAACTTACAG	GCCCTTTTGT

GACAAAATAA CTGTTTTATT	CACCTTTATG GTGGAAATAC	HindIII ~ AGTCTTGATA TCAGAACTAT	
ntinued) TATTGATTGT ATAACTAACA	TATATGTTGC ATATACAACG	CGTAATAAGG	
ditional pCAL vector modules and pCAL vectors (continued) GGTAAAACCCT ATGAATTTTC TATTGATTGT CCATTTGGGA TACTTAAAAG ATAACTAACA	GCGTTTCTTT CGCAAAGAAA	CTACGTTTGC TAACATACTG GATGCAAACG ATTGTATGAC	
dditional pCAL vector mod GGTAAACCCT CCATTTGGGA	TGGTGTCTTT	CTACGTTTGC TAACATACTG GATGCAAACG ATTGTATGAC	
Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) 1101 CTTTGGCGCT GGTAAACCCT ATGAATTTTC TATT GAAACCGCGA CCATTTGGGA TACTTAAAAG ATAA	ACTTATTCCG TGAATAAGGC	TATGTATTTT ATACATAAAA	HindI ~~~~ AGCTT TCGAA
Figure 35a: Functiona 1101	1151	1201	UBSTITUTE SHEET (RULE 26)

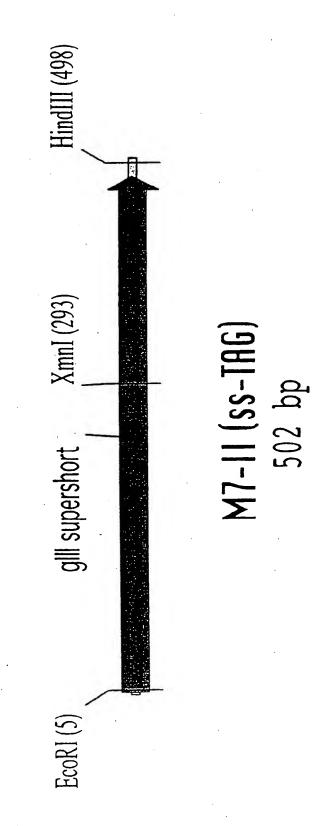


Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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11111				
 CGGGAATTCG	GAGGCGGTTC	CGGTGGTGGC	TCTGGTTCCG	GTG.
GCCCTTAAGC	CTCCGCCAAG	G GCCACCACCG AGACCAAGGC	AGACCAAGGC	CAC

GAAAATGCCG	CTTTTACGGC
S CTAATAAGGG GGCTATGACC GAAAATGCCG	TACCGITIGG GATIATICCC CCGATACIGG CITITACGGC
CTAATAAGGG	GATTATTCCC
ATGGCAAACG	TACCGTTTGC
TTATGAAAAG	ATACTTTTC
51	

GTTTTACGGC	TTCTGTCGCT
AIGECARACE CIRAIRAGEE GECIAIGACE GARAGIGCEE TACCETTIGE GATTATICCE CCGATACTEG CTTTTACGGC	GCTACAGTCT GACGCTAAAG GCAAACTTGA TTCTGTCGCT CGATGTCAGA CTGCGATTTC CGTTTGAACT AAGACAGCGA
GATTATTCCC	GACGCTAAAG CTGCGATTTC
TACCGTTTGC	GCTACAGTCT CGATGTCAGA
AATACTTTTC	ATGAAAACGC TACTTTTGCG
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TTTCCGGCCT	AATTCCCAAA
AAAGGCCGGA	TTAAGGGTTT
ATTGGTGACG	CTGGTGATTT TGCTGGCTCT
TAACCACTGC	GACCACTAAA ACGACCGAGA
CGATGGTTTC	CTGGTGATTT
GCTACCAAAG	GACCACTAAA
GTGCTGCTAT	AATGGTGCTA TTACCACGAT
ACTGATTACG	TGCTAATGGT
TGACTAATGC	ACGATTACCA
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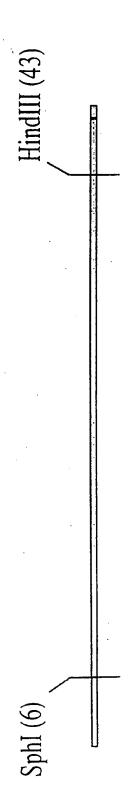
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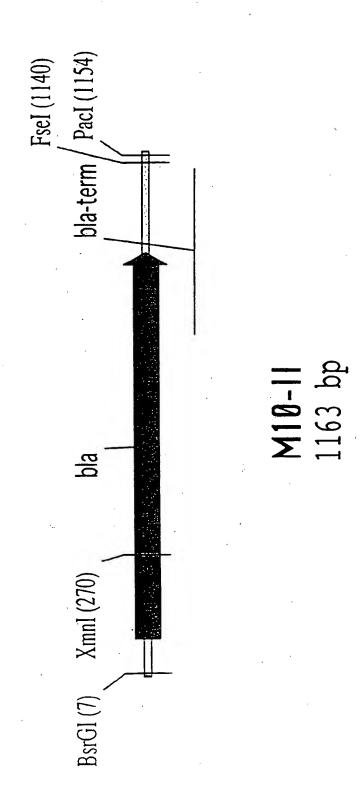
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HindIII CTTGATAAGC GAACTATTCG	AATAAGGAGT TTATTCCTCA	CATACTGCGT GTATGACGCA	CGTTTGCTAA GCAAACGATT	GTATTTTCTA CATAAAAGAT	451
CTTTATGTAT GAAATACATA	ATGTTGCCAC TACAACGGTG	TTTCTTTTAT AAAGAAAATA	TGTCTTTGCG	TATTCCGTGG	401
AAAATAAACT TTTTATTTGA	TGATTGTGAC AAAATAAACT ACTAACACTG TTTTATTTGA	AATTTTCTAT TTAAAAGATA	AAACCATATG TTTGGTATAC	TGGCGCTGGT	351
CTTTTGTCTT GAAAACAGAA	GAATGTCGCC CTTACAGCGG	TCAATCGGTT AGTTAGCCAA	CTTCCCTCCC	CAATATTTAC GTTATAAATG	301



**X8** 47 bp

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		TACGAAGTTA	ATGCTTCAAT
		ATGTACGCTA	TACATGCGAT
		ACTICGIATA AIGIACGCIA	GGTAT TGAAGCATAT TACATGCGAT ATGCTTCAAT
Tuds	***************************************	GCATGCCATA	CGTACGGTAT



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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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: ATGAGACAAT AACCCTGATA	ACTCTGTTA TTGGGACTAT
C ATTCAAATAT GTATCCGCTC A	G TAAGTTTATA CATAGGCGAG TACTCTGTTA T
ATTCAAATAT	TAAGTTTATA
GGGGGTGTAC	CCCCCACATG

CAACATTTCC	GTTGTAAAGG
TATGAGTATT	S ATACTCATAA
AAGGAAGAG	TTCCTTCT
TAATATTGAA	ATTATAACTT I
LTCAA	TTACGAAGTT
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AGTTGGGTGC	S TCAACCCACG
SCTGAGGATC	CGACTCCTA
AGTAAAAGAT (	TCATTTTCTA
CGCTGGTGAA	GCGACCACTT
ACCCAGAAA	GTGGGTCTTT
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GGT TACATCGAAC TGGATCTCAA CAGCGGTAAG ATCCTTGAGA	A ATGTAGCTTG ACCTAGAGTT GTCGCCATTC TAGGAACTC
CAGCGGTAAG	GTCGCCATTC
TGGATCTCAA	ACCTAGAGTT
TACATCGAAC	ATGTAGCTTG
GCGAGTGGGT	CGCTCACCCA
201	

#### XmnI

TAAAGTTCTC	ATTTCAACAC
TGAGCACTTT	GCTTCTTGCA AAAGGTTACT ACTCGTGAAA
TTTCCAATGA	AAAGGTTACT
CGAAGAACGT	GCTTCTTGCA
GTTTTCGCCC	CAAAAGCGGG
251	

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

301 CTATGTGGCG GATACACCGC	351 TCGCCGCATA AGCGGCGTAT	401 CAGAAAAGCA GTCTTTTCGT	451 GCCATAACCA CGGTATTGGT	501 CGGAGGACCG GCCTCCTGGC	551 TAACTCGCCT ATTGAGCGGA	601 GACGAGCGTG CTGCTCGCAC	651 ACTATTAACT TGATAATTGA
2522	CATA GTAT	AGCA	ACCA	ACCG TGGC	GCCT	CGTG	AACT
CGGTATTATC GCCATAATAG	CACTATTCTC GTGATAAGAG	TCTTACGGAT AGAATGCCTA	TGAGTGATAA ACTCACTATT	AAGGAGCTAA TTCCTCGATT	TGATCGTTGG ACTAGCAACC	ACACCACGAT TGTGGTGCTA	GGCGAACTAC CCGCTTGATG
CCGTATTGAC GGCATAACTG	AGAATGACTT TCTTACTGAA	GGCATGACAG	CACTGCGGCC GTGACGCCGG	CCGCTTTTTT GGCGAAAAAA	GAACCGGAGC CTTGGCCTCG	GCCTGTAGCA	TTACTCTAGC AATGAGATCG
GCCGGGCAAG	GGTTGAGTAC CCAACTCATG	TAAGAGAATT ATTCTCTTAA	AACTTACTTC TTGAATGAAG	GCACAACATG CGTGTTGTAC	TGAATGAAGC ACTTACTTCG	ATGGCAACAA TACCGTTGTT	TICCCGGCAA
AGCAACTCGG TCGTTGAGCC	TCACCAGTCA AGTGGTCAGT	ATGCAGTGCT TACGTCACGA	TGACAACGAT ACTGTTGCTA	GGGGATCATG	CATACCAAAC GTATGGTTTG	CGTTGCGCAA GCAACGCGTT	CAGTTAATAG GTCAATTATC
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

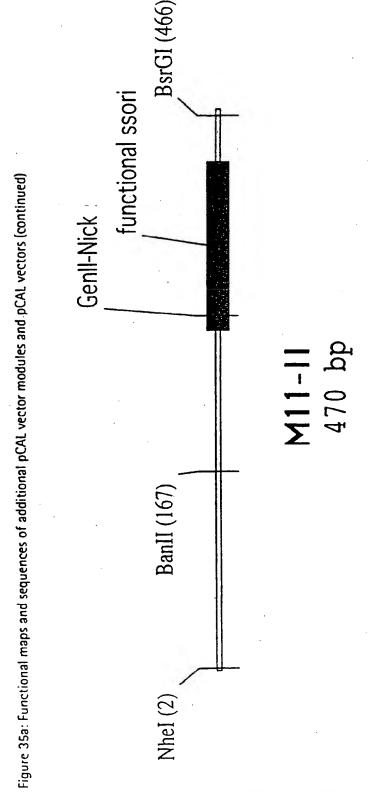
	701	ACTGGATGGA TGACCTACCT	GGCGGATAAA CCGCCTATTT	GTTGCAGGAC	CACTTCTGCG	CTCGGCCCTT
	751	CCGGCTGGCT	GGTTTATTGC CCAAATAACG	TGATAAATCT ACTATTTAGA	GGAGCCGGTG CCTCGGCCAC	AGCGTGGGTC
	801	TCGCGGTATC AGCGCCATAG	ATTGCAGCAC TAACGTCGTG	TGGGGCCAGA	TGGTAAGCCC ACCATTCGGG	TCCCGTATCG
Ounc	851	TAGTTATCTA ATCAATAGAT	CACGACGGGG GTGCTGCCCC	AGTCAGGCAA TCAGTCCGTT	CTATGGATGA GATACCTACT	ACGAAATAGA TGCTTTATCT
	901	CAGATCGCTG GTCTAGCGAC	AGATAGGTGC TCTATCCACG	CTCACTGATT GAGTGACTAA	AAGCATTGGG	TAACTGTCAG ATTGACAGTC
	951	ACCAAGTTTA TGGTTCAAAT	CTCATATATA GAGTATATAT	CTTTAGATTG GAAATCTAAC	ATTTAAAACT TAAATTTTGA	TCATTTTAA AGTAAAAATT
	1001	TTTAAAAGGA AAATTTTCCT	TCTAGGTGAA AGATCCACTT	GATCCTTTTT CTAGGAAAAA	GATAATCTCA CTATTAGAGT	TGACCAAAAT ACTGGTTTTA
1-11	1051	CCCTTAACGT GGGAATTGCA	GAGTTTTCGT	TCCACTGAGC AGGTGACTCG	GTCAGACCCC CAGTCTGGGG	GTAGAAAAGA CATCTTTTCT

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1101	TCAAAGGATC AGTTTCCTAG	TTCTTGAGAT AAGAACTCTA	CCTTTTTGAT GGAAAAACTA	AATGGCCGGC TTACCGGCCG	CCCCCCCTT	
	PacI					
	1 2 2 2 1		*			
1151	AATTAAGGGG	999				

TTAATTCCCC CCC



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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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н	GCTAGCACGC CGATCGTGCG	GCCCTGTAGC CGGGACATCG	GGCGCATTAA CCGCGTAATT	2229229292 222929292929	TGTGGTGGTT
51	ACGCGCAGCG	TGACCGCTAC ACTGGCGATG	ACTTGCCAGC TGAACGGTCG	GCCCTAGCGC CGGGATCGCG	CCGCTCCTTT GGCGAGGAAA
101	CGCTTTCTTC GCGAAAGAAG	CCTTCCTTTC GGAAGGAAAG	TCGCCACGTT AGCGGTGCAA	CGCCGGCTTT	CCCCGTCAAG
151	CTCTAAATCG	Banii	TTAGGGTTCC	GATTTAGTGC	TTTACGGCAC
201	GAGATTTAGC	CCCCGAGGGA	AATCCCAAGG	CTAAATCACG	AAATGCCGTG GTGGGCCATC
251	GAGCTGGGGT GCCCTGATAG CGGGACTATC	TTTTTGAACT ACGGTTTTTC TGCCAAAAAG	AATCCCACTA GCCCTTTGAC CGGGAAACTG	CCAAGAGCAT CACCCGGTAG GTTGGAGTCC ACGTTCTTTA CAACCTCAGG TGCAAGAAAT	CACCCGGTAG ACGTTCTTTA TGCAAGAAAT

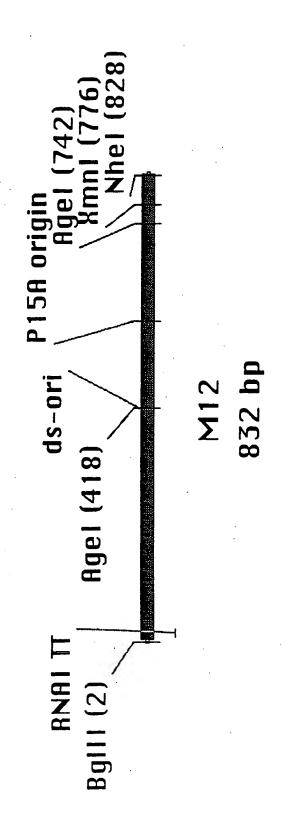
jure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)	SOCKKUBUKU KANAKUUBUK KANDEBUUBU BUKUUBUKEK 100
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301	ATAGTGGACT TATCACCTGA	CTTGTTCCAA GAACAAGGTT	CTTGTTCCAA ACTGGAACAA CACTCAACCC GAACAAGGTT TGACCTTGTT GTGAGTTGGG		TATCTCGGTC ATAGAGCCAG
351	TATTCTTTG	ATTTATAAGG	ATTTATAAGG GATTTTGCCG ATTTCGGCCT	GATTTTGCCG ATTTCGGCCT ATTGGTTAAA	ATTGGTTAAA
	ATAAGAAAAC	TAAATATTCC	TAAATATTCC CTAAAACGGC TAAAGCCGGA	CTAAAAACGGC TAAAGCCGGA TAACCAATTT	TAACCAATTT
401	AAATGAGCTG	ATTTAACAAA	AATTTAACGC	ATTTAACAAA AATTTAACGC GAATTTTAAC AAAATATTAA	AAAATATTAA
	TTTACTCGAC	TAAATTGTTT	TTAAATTGCG	TAAATTGTTT TTAAATTGCG CTTAAAATTG TTTTATAATT	TTTTATAATT

BsrGI

TTCATGTACA AAGTACATGT 11111 GCAAATGTTA CGTTTACAAT

451



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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)	12: Bglii	~~~~~~~~   AGATCTAATA AGATGATCTT CTTGAGATCG TTTTGGTCTG CGCGTAATCT TCTAGATTAT TCTACTAGAA GAACTCTAGC AAAACCAGAC GCGCATTAGA	L CTTGCTCTGA AAACGAAAAA ACCGCCTTGC AGGGCGGTTT TTCGTAGGTT GAACGAGACT TTTGCTTTTT TGGCGGAACG TCCCGCCAAA AAGCATCCAA	L CTCTGAGCTA CCAACTCTTT GAACCGAGGT AACTGGCTTG GAGGAGCGCA GAGACTCGAT GGTTGAGAAA CTTGGCTCCA TTGACCGAAC CTCCTCGCGT	1 GTCACTAAAA CTTGTCCTTT CAGTTTAGCC TTAACCGGCG CATGACTTCA CAGTGATTTT GAACAGGAAA GTCAAATCGG AATTGGCCGC GTACTGAAGT	1 AGACTAACTC CTCTAAATCA ATTACCAGTG GCTGCTGCCA GTGGTGCTTT TCTGATTGAG GAGATTTAGT TAATGGTCAC CGACGACGGT CACCACGAAA	1 TGCATGTCTT TCCGGGTTGG ACTCAAGACG ATAGTTACCG GATAAGGCGC ACGTACAGAA AGGCCCAACC TGAGTTCTGC TATCAATGGC CTATTCCGCG	1 AGCGGTCGGA CTGAACGGGG GGTTCGTGCA TACAGTCCAG CTTGGAGCGA TCGCCAGCCT GACTTGCCCC CCAAGCACGT ATGTCAGGTC GAACCTCGCT
unctional m	••	AGA' TCT.	CTT	CTC	GTC	AGA TCT	TGC ACG	AGC TCG
Figure 35a: F	Z	₽	51	TO T	TE SHEET (	20 J	251	301
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CAGTGAGCGA

CGTAGCGAGT

AACGACCGAG TTGCTGGCTC

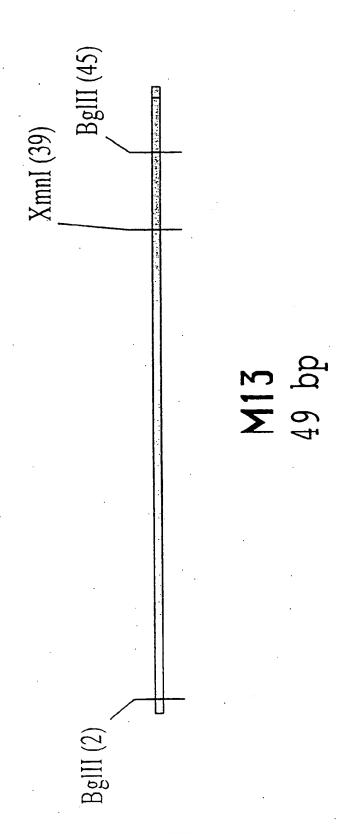
CGGCGTCAGC

TAAAGGCGAG

TTTGCGCCGG AAACGCGGCC CCTTACTCTG GGAATGAGAC Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) ACAGTCCGCA TGTCAGGCGT GCCTTGACTC CGGAACTGAG TGACGGATGG ACTGCCTACC 351

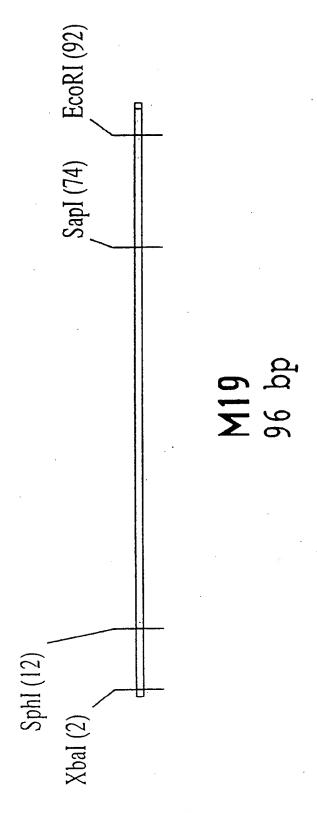
		AGGCAGGAAC AGGAGAGCGC TCCGTCCTTG TCCTCTCGCG	TATCTTTATA GTCCTGTCGG ATAGAAATAT CAGGACAGCC	TTCGTGATGC TTGTCAGGGG AAGCACTACG AACAGTCCCC	CGGCCCTCTC ACTTCCCTGT GCCGGGAGAG TGAAGGGACA	CTCCGCCCCG TTCGTAAGCC GAGGCGGGC AAGCATTCGG	CGTAGCGAGT CAGTGAGCGA
AgeI	AgeI	GTAAACCGAA CATTTGGCTT	AAACGCCTGG TTTGCGGACC	AGCGTCAGAT TCGCAGTCTA	GGCTTTGCCG CCGAAACGGC	TCCAGGAAAT AGGTCCTTTA	GCCGCAGTCG AACGACCGAG CG
		ATAACAGCGG AATGACACCG TATTGTCGCC TTACTGTGGC	AGGAGGGAGC CGCCAGGGGG TCCTCCCTCG GCGGTCCCCC	GTTTCGCCAC CACTGATTTG CAAAGCGGTG GTGACTAAAC	GGCGGAGCCT ATGGAAAAC CCGCCTCGGA TACCTTTTG	TAAGTATCTT CCTGGCATCT ATTCATAGAA GGACCGTAGA	ATTTCCGCTC GCCGCAG
		401 AS	451 A(	501 67	551 GC	601 TZ	651 A

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)



M 13:

BglII TTCAGATCT AAGTCTAGA ATGCTTCAAT TACGAAGTTA XmnI ATGTATGCTA TACATACGAT ACTTCGTATA TGAAGCATAT AGATCTCATA TCTAGAGTAT BglII 11111



CTATTGCACT GATAACGTGA

TTTGTTTCGT

TTTATTTAC

CGCATCCTCT

AGATCTCGTA

ECORI

19: Σ

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

SphI XbaI

AAACAAAGCA AAATAAAATG GCGTAGGAGA TCTAGAGCAT 11111

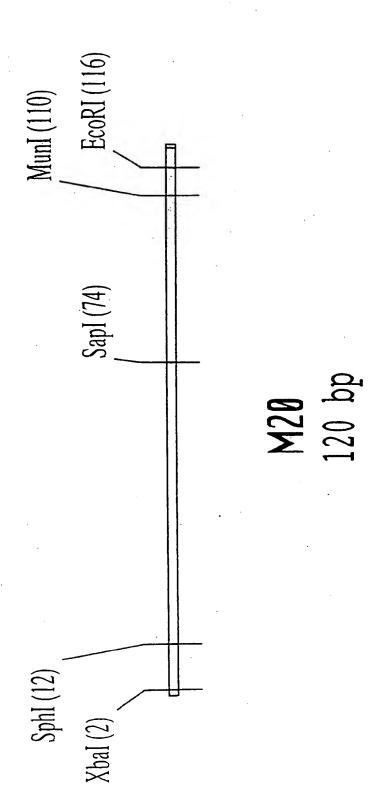
SapI

GAATTC TACCAAAGCC TCACCCCTGT CCGTTGCTCT

CTTAAG ATGGTTTCGG AGTGGGGACA GGCAACGAGA GGCACTCTTA CCGTGAGAAT

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M 20:

XbaI SphI

CTATTGCACT GATAACGTGA AAACAAAGCA TTTGTTTCGT AAATAAAATG TTTATTTAC GCGTAGGAGA CGCATCCTCT TCTAGAGCAT AGATCTCGTA

SapI

GACTACAAAG CTGATGTTTC TACCAAAGCC ATGGTTTCGG TCACCCCTGT AGTGGGGACA CCGTTGCTCT GGCAACGAGA CCGTGAGAAT GGCACTCTTA

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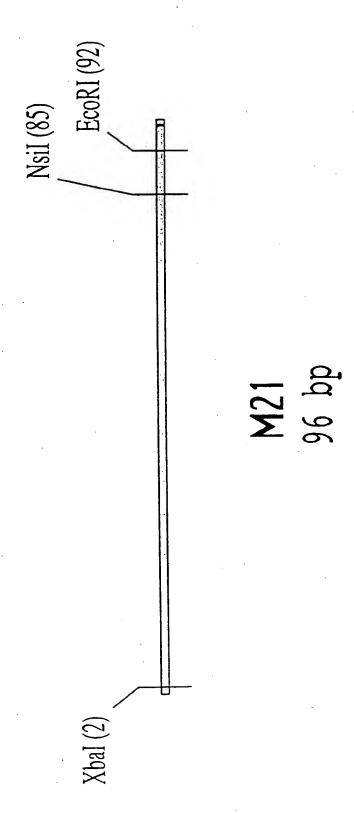
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ATGAAGTGCA ATTGGAATTC TACTTCACGT TACCTTAAG

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21 Σ XbaI

11111

TTCTTGC AAGAAGAACG TTATAGCGTA AATATCGCAT TATGAAAAAG ATACTTTTC GAGGTGATTT CTCCACTAAA TCTAGAGGTT AGATCTCCAA

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GAATTC

CTTAAG ACGTATGCGA TGCATACGCT TTGCTACAAA AACGATGTTT

TAGATACAAG 51

ATCTATGTTC

GTTTTTCTA CAAAAAAGAT

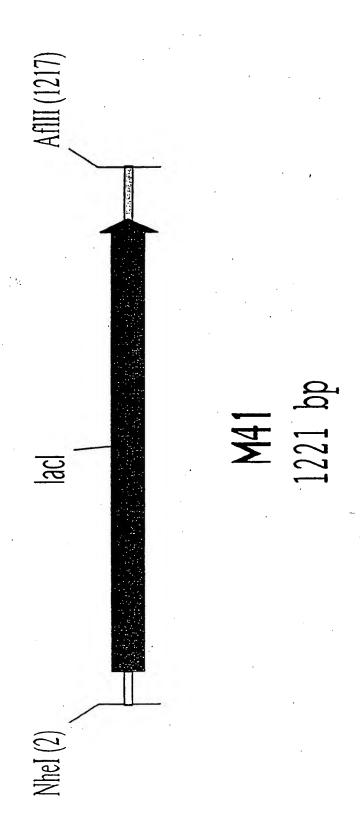


Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

M 41:

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| П | GCTAGCATCG
CGATCGTAGC | AATGGCGCAA
TTACCGCGTT | AACCTTTCGC
TTGGAAAGCG | GGTATGGCAT
CCATACCGTA | GATAGCGCCC
CTATCGCGGG | |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---|
| 51 | GGAAGAGAGT
CCTTCTCTCA | CAATTCAGGG
GTTAAGTCCC | TGGTGAATGT
ACCACTTACA | GAAACCAGTA
CTTTGGTCAT | ACGTTATACG
TGCAATATGC | |
| 101 | ATGTCGCAGA
TACAGCGTCT | GTATGCCGGT | GTCTCTTATC
CAGAGAATAG | AGACCGTTTC
TCTGGCAAAG | CCGCGTGGTG
GGCGCACCAC | • |
| 151 | AACCAGGCCA
TTGGTCCGGT | GCCACGTTTC
CGGTGCAAAG | TGCGAAAACG
ACGCTTTTGC | CGGGAAAAAG
GCCCTTTTTC | TGGAAGCGGC
ACCTTCGCCG | |
| 201 | GATGGCGGAG | CTGAATTACA
GACTTAATGT | TTCCTAACCG
AAGGATTGGC | CGTGGCACAA
GCACCGTGTT | CAACTGGCGG
GTTGACCGCC | |
| 251 | GCAAACAGTC | GTTGCTGATT
CAACGACTAA | GGCGTTGCCA
CCGCAACGGT | CCTCCAGTCT
GGAGGTCAGA | GGCCCTGCAC | |
| 301 | GCGCCGTCGC | AAATTGTCGC
TTTAACAGCG | GGCGATTAAA
CCGCTAATTT | TCTCGCGCCG | ATCAACTGGG
TAGTTGACCC | |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| 351 | TGCCAGCGTG
ACGGTCGCAC | GTCGTGTCGA | TGGTAGAACG
ACCATCTTGC | AAGCGGCGTC
TTCGCCGCAG | GAAGCCTGTA
CTTCGGACAT |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 401 | AAGCGGCGGT | GCACAATCTT | CTCGCGCAAC | GTGTCAGTGG | GCTGATTATT |
| | TTCGCCGCCA | CGTGTTAGAA | GAGCGCGTTG | CACAGTCACC | CGACTAATAA |
| 451 | AACTATCCGC | TGGATGACCA | GGATGCTATT | GCTGTGGAAG | CTGCCTGCAC |
| | TTGATAGGCG | ACCTACTGGT | CCTACGATAA | CGACACCTTC | GACGGACGTG |
| 501 | TAATGTTCCG | GCGTTATTTC | TTGATGTCTC | TGACCAGACA | CCCATCAACA |
| | ATTACAAGGC | CGCAATAAAG | AACTACAGAG | ACTGGTCTGT | GGGTAGTTGT |
| 551 | GTATTATTT
CATAATAAAA | CTCCCATGAG
GAGGGTACTC | GACGGTACGC | GACTGGGCGT
CTGACCCGCA | GGAGCATCTG
CCTCGTAGAC |
| 601 | GTCGCATTGG
CAGCGTAACC | GCCACCAGCA | AATCGCGCTG
TTAGCGCGAC | TTAGCTGGCC
AATCGACCGG | CATTAAGTTC
GTAATTCAAG |
| 651 | TGTCTCGGCG | CGTCTGCGTC
GCAGACGCAG | TGGCTGGCTG | GCATAAATAT
CGTATTTATA | CTCACTCGCA
GAGTGAGCGT |
| 701 | ATCAAATTCA | GCCGATAGCG | GAACGGGAAG | GCGACTGGAG | TGCCATGTCC |
| | TAGTTTAAGT | CGGCTATCGC | CTTGCCCTTC | CGCTGACCTC | ACGGTACAGG |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| 751 | GGTTTTCAAC
CCAAAAGTTG | AAACCATGCA
TTTGGTACGT | AATGCTGAAT
TTACGACTTA | GAGGCCATCG
CTCCCGTAGC | TTCCCACTGC
AAGGGTGACG |
|------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 801 | GATGCTGGTT
CTACGACCAA | GCCAACGATC
CGGTTGCTAG | AGATGGCGCT
TCTACCGCGA | GGGCGCAATG | CGTGCCATTA
GCACGGTAAT |
| 851 | CCGAGTCCGG | GCTGCGCGTT
CGACGCGCAA | GGTGCGGACA
CCACGCCTGT | TCTCGGTAGT
AGAGCCATCA | GGGATACGAC
CCCTATGCTG |
| 901 | GATACCGAGG
CTATGGCTCC | ACAGCTCATG
TGTCGAGTAC | TTATATCCCG
AATATAGGGC | CCGCTGACCA
GGCGACTGGT | CCATCAAACA
GGTAGTTTGT |
| 951 | GGATTTTCGC
CCTAAAAGCG | CTGCTGGGGC | AAACCAGCGT
TTTGGTCGCA | GGACCGCTTG
CCTGGCGAAC | CTGCAACTCT
GACGTTGAGA |
| 1001 | CTCAGGGCCA
GAGTCCCGGT | GGCGGTGAAG | GGCAATCAGC | TGTTGCCCGT
ACAACGGGCA | CTCACTGGTG
GAGTGACCAC |
| 1051 | AAAAGAAAAA
TTTTCTTTTT | CCACCCTGGC | TCCCAATACG | CAAACCGCCT
GTTTGGCGGA | CTCCCCGCGC |
| 1101 | GTTGGCCGAT | TCACTGATGC
AGTGACTACG | AGCTGGCACG
TCGACCGTGC | ACAGGTTTCC
TGTCCAAAGG | CGACTGGAAA
GCTGACCTTT |

GGAGGCCGTT CCTCCGGCAA CTTCCTGACA TATTTTCGCC GAAGGACTGT ATAAAAGCGG AGGCTACCCG TCCGATGGGC GCGGCCAGTG CGCCCGTCAC 1151

Aflii

GCCCACTTAA TTGTTTGCA

 \mathcal{O} CGGGTGAATT AACAAAACGT

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Hind111 (994) lac p/o Kbal (937) Sphl (957) lpp-Terminator **Hatll** (896) Pacl (1058) Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) cat Fsel (1078) Bg111 (1) 2380 bp pCALO-Bsr61 (1091) RNAI TI functional ssori GenII-Nick ds-ori P15A origin Ban11 (1398) 8mn! (1611) Nhel (1555) Age! (1641) **Agel (1965)**

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ectors (continued)

| Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL ve
pCALO-1:
BglII | pCAL vector modules and pCAL ve |
|--|---------------------------------|
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| | |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| 351 | TATGTGTAGA
ATACACATCT | AACTGCCGGA AATCGTCGTG
TTGACGGCCT TTAGCAGCAC | AACTGCCGGA AATCGTCGTG GTATTCACTC CAGAGCGATG
TTGACGGCCT TTAGCAGCAC CATAAGTGAG GTCTCGCTAC | GTATTCACTC CAGAGCGATG
CATAAGTGAG GTCTCGCTAC | CAGAGCGATG
GTCTCGCTAC | |
|-----|--------------------------|--|--|--|--------------------------|--|
| 401 | AAAACGTTTC
TTTTGCAAAG | AGTTTGCTCA
TCAAACGAGT | AGTTTGCTCA TGGAAAACGG TGTAACAAGG GTGAACACTA
TCAAACGAGT ACCTTTTGCC ACATTGTTCC CACTTGTGAT | TGTAACAAGG
ACATTGTTCC | GTGAACACTA
CACTTGTGAT | |
| 451 | TCCCATATCA | CCAGCTCACC | CCAGCTCACC GTCTTTCATT GCCATACGGA ACTCCGGGTG
GGTCGAGTGG CAGAAAGTAA CGGTATGCCT TGAGGCCCAC | GCCATACGGA
CGGTATGCCT | ACTCCGGGTG
TGAGGCCCAC | |

| TAAAACTTGT | CAGCTGAACG |
|---|------------|
| ATTTTGAACA | GTCGACTTGC |
| AGGCGGGCAA GAATGTGAAT AAAGGCCGGA TAAAACTTGT | CCGTAATATC |
| TCCGCCCGTT CTTACACTTA TTTCCGGCCT ATTTTGAACA | GGCATTATAG |
| GAATGTGAAT | TTTAAAAAGG |
| CTTACACTTA | AAATTTTTCC |
| AGGCGGGCAA | CTTTACGGTC |
| TCCGCCCGTT | GAAATGCCAG |
| AGCATTCATC | GCTTATTTTT |
| TCGTAAGTAG | CGAATAAAAA |
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| CAAAATGTTC | GTTTTACAAG |
|--|--|
| AT AGGTACATTG AGCAACTGAC TGAAATGCCT CAAAATGTTC | TA TCCATGIAAC TCGTTGACTG ACTTTACGGA GTTTTACAAG |
| AGCAACTGAC | TCGTTGACTG |
| AGGTACATTG | TCCATGTAAC |
| GTCTGGTTAT | CAGACCAATA |
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| GTGATTTTT | CACTAAAAAA |
|--------------|------------|
| GGTATATCCA | CCATATAGGT |
| A TATCAACGGT | ATAGTTGCCA |
| CATTGGGATA | GTAACCCTAT |
| TTTACGATGC | AAATGCTACG |
| 651 | |

| CTCAAAAAT | GAGTTTTTA |
|------------|------------|
| ATCTCGATAA | TAGAGCTATT |
| GCTCCTGAAA | CGAGGACTTT |
| AGCTTCCTTA | TCGAAGGAAT |
| TCTCCATTTT | AGAGGTAAAA |
| 701 | |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| | • | | | | | | |
|--------------------------|--|--------------------------|--------|--------------------------|---------|--------------------------|--------------------------|
| AACCTCACCC
TTGGAGTGGG | GCTTTACACT
CGAAATGTGA | ATAACAATTT
TATTGTTAAA | į | ACCCCCCCCC | HindIII | ATAAGCTTGA
TATTCGAACT | TTTGTCTGCC |
| TGAAAGTTGG
ACTTTCAACC | GGCACCCCAG
CCGTGGGGTC | TTGTGAGCGG | Xbal | GAATTTCTAG | | ATACGAAGTT
TATGCTTCAA | CGACATTTTT
GCTGTAAAAA |
| TTCATTATGG
AAGTAATACC | TCACTCATTA
AGTGAGTAAT | TTGTGTGGAA | | CCATGATTAC
GGTACTAATG | | AATGTACGCT
TTACATGCGA | GCAGATTGTG
CGTCTAACAC |
| GTGATCTTAT
CACTAGAATA | GTGAGTTAGC
CACTCAATCG | GGCTCGTATG
CCGAGCATAC | • | ACAGCTATGA
TGTCGATACT | | AACTTCGTAT
TTGAAGCATA | GAAAAATGGC
CTTTTTACCG |
| ACGCCCGGTA | Aatli
~~~~~
GACGTCTAAT
CTGCAGATTA | TTATGCTTCC
AATACGAAGG | | CACACAGGAA
GTGTGTCCTT | SphI | CGCATGCCAT
GCGTACGGTA | CCTGTGAAGT
GGACACTTCA |
| 751 ACGCCO | 801 | 851 | TO! TE | O 0 1 | F 03) | 951 | 1001 |
| į | | 0000 | 111016 | الماسان (داعات | 0] | | |

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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| BsrGI | GTACATGAAA
CATGTACTTT | TTGTTAAATC
AACAATTTAG | CTTATAAATC
GAATATTTAG | TGGAACAAGA
ACCTTGTTCT | AAAAACCGTC
TTTTTGGCAG | CAAGTTTTTT
GTTCAAAAAA | Banll | GGGAGCCCCC |
|-------|--------------------------|--------------------------|--------------------------|--------------------------|--|--------------------------|-------|--------------------------|
| | GGGGGGGGGT | CGTTAAATTT
GCAATTTAAA | GGCAAAATCC
CCGTTTTAGG | TGTTCCAGTT
ACAAGGTCAA | TCAAAGGGCG
AGTTTCCCGC | TCACCCTAAT
AGTGGGATTA | | GAACCCTAAA
CTTGGGATTT |
| FseI | GGGCCGGCCT | TTAAAATTCG | GGCCGAAATC
CCGGCTTTAG | GGTTGAGTGT
CCAACTCACA | GACTCCAACG
CTGAGGTTGC | ACGAGAACCA
TGCTCTTGGT | | CACTAAATCG
GTGATTTAGC |
| | AGGGGGGGGG
TCCCCCCCC | TAATATTTTG
ATTATAAAAC | TTAACCAATA
AATTGGTTAT | ACCGAGATAG
TGGCTCTATC | GTCCACTATT AAAGAACGTG
CAGGTGATAA TTTCTTGCAC | ATGGCCCACT | · | TGCCGTAAAG
ACGGCATTTC |
| PacI | GTTTAATTAA
CAAATTAATT | TTGTAAACGT
AACATTTGCA | AGCTCATTTT
TCGAGTAAAA | AAAAGAATAG
TTTTCTTATC | GTCCACTATT
CAGGTGATAA | TATCAGGGCG | | GGGGTCGAGG |
| | 1051 | 1101 | 1151 | 1201 | 1251 | 1301 | | 1351 |

| TGCTTGCCCC | GAAGTGAGAG
CTTCACTCTC | GACAAGCATC
CTGTTCGTAG | AGGACTATAA
TCCTGATATT | CTCCTGTTCC
GAGGACAAGG | | CGTTTGTCTC
GCAAACAGAG | CCAAGCTGGA
GGTTCGACCT | TTATCCGGTA
AATAGGCCAT |
|--|--------------------------|--------------------------|--------------------------|--------------------------|------|--------------------------|--------------------------|--------------------------|
| TACCGAA | ACTTAACAGG
TGAATTGTCC | CCGCCCCCT | GAAACCCGAC
CTTTGGGCTG | CTCCTGCGCT
GAGGACGCGA | | GTTATGGCCG
CAATACCGGC | GCAGTTCGCT
CGTCAAGCGA | CCGCTGCGCC |
| <u> </u> | CCAGGAAGAT
GGTCCTTCTA | TCCATAGGCT
AGGTATCCGA | CAGTGGTGGC
GTCACCACCG | TGGCGGCTCC | | TCATTCCGCT
AGTAAGGCGA | TTCCGGGTAG | TTCAGTCCGA |
| litional pCAL vector modules and pCAL vectors (cc
AGCAAGCTGA CGCCGCTCGC | CTGGAAGATG
GACCTTCTAC | AAGCCGTTTT
TTCGGCAAAA | ACGCTCAAAT
TGCGAGTTTA | CGTTTCCCCC | AgeI | TTTACCGGTG
AAATGGCCAC | TGACACTCAG | GAACCCCCCG |
| Figure 35a: Functional maps and sequences of add | CGGAGATTTC | GGCCGCGGCA | ACGAAATCTG
TGCTTTAGAC | AGATACCAGG
TCTATGGTCC | | TGCCTTTCGG
ACGGAAAGCC | ATTCCACGCC
TAAGGTGCGG | CTGTATGCAC
GACATACGTG |
| a: Functional | 1751 | 1801 | 1851 | 1901 | | 1951 | 2001 | 2051 |
| Figure 35 | | | SUE | 3STITUTE SH
161 / 2 | | LE 26) | | |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

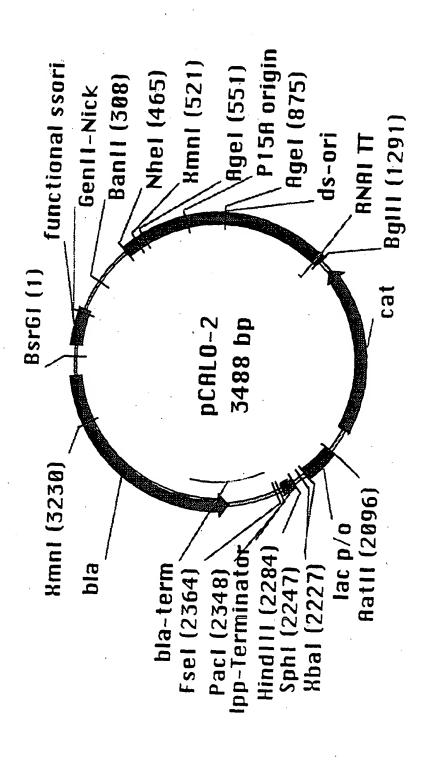
| | 1401 | GATTTAGAGC
CTAAATCTCG | TTGACGGGGA
AACTGCCCCT | AAGCCGGCGA
TTCGGCCGCT | ACGTGGCGAG
TGCACCGCTC | AAAGGAAGGG
TTTCCTTCCC |
|------|------|--|--------------------------|--------------------------|--------------------------|--------------------------|
| | 1451 | AAGAAAGCGA
TTCTTTCGCT | AAGGAGCGGG
TTCCTCGCCC | CGCTAGGGCG
GCGATCCCGC | CTGGCAAGTG
GACCGTTCAC | TAGCGGTCAC
ATCGCCAGTG |
| | 1501 | GCTGCGCGTA | ACCACCACAC
TGGTGGTGTG | CCGCCGCGCT | TAATGCGCCG
ATTACGCGGC | CTACAGGGCG
GATGTCCCGC |
| | 1551 | Nhel
~~~~~~
CGTGCTAGCG
GCACGATCGC | GAGTGTATAC
CTCACATATG | TGGCTTACTA | TGTTGGCACT
ACAACCGTGA | GATGAGGGTG |
| CHIE | | IcmX | It | | | AgeI |
| 00) | 1601 | TCAGTGAAGT OAGT OAGT | GCTTCATGTG | GCAGGAGAAA
CGTCCTCTTT | AAAGGCTGCA
TTTCCGACGT | CCGGTGCGTC |
| | 1651 | AGCAGAATAT
TCGTCTTATA | GTGATACAGG
CACTATGTCC | ATATATTCCG
TATATAAGGC | CTTCCTCGCT | CACTGACTCG |
| | 1701 | CTACGCTCGG | TCGTTCGACT | GCGGCGAGCG | GAAATGGCTT | ACGAACGGGG |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| | 2101 | ACTATCGTCT
TGATAGCAGA | TGAGTCCAAC
ACTCAGGTTG | CCGGAAAGAC
GGCCTTTCTG | ATGCAAAAGC
TACGTTTTCG | ACCACTGGCA
TGGTGACCGT | |
|------------|--------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--|
| | 2151 | GCAGCCACTG
CGTCGGTGAC | GTAATTGATT
CATTAACTAA | TAGAGGAGTT | AGTCTTGAAG
TCAGAACTTC | TCATGCGCCG
AGTACGCGGC | |
| ` (| 2201 | GTTAAGGCTA
CAATTCCGAT | AACTGAAAGG
TTGACTTTCC | ACAAGTTTTA
TGTTCAAAAT | GTGACTGCGC
CACTGACGCG | TCCTCCAAGC
AGGAGGTTCG | |
| SUBSTITUTE | 2251 | CAGTTACCTC
GTCAATGGAG | GGTTCAAAGA
CCAAGTTTCT | GTTGGTAGCT | CAGAGAACCT
GTCTCTTGGA | ACGAAAAACC
TGCTTTTTGG | |
| SHEET (RU | . 2301 | GCCCTGCAAG
CGGGACGTTC | GCGGTTTTTT
CGCCAAAAAA | CGTTTTCAGA
GCAAAAGTCT | GCAAGAGATT
CGTTCTCTAA | ACGCGCAGAC
TGCGCGTCTG | |
| LE 26) | | | | BglII | | | |
| | 2351 | CAAAACGATC
GTTTTGCTAG | TCAAGAAGAT
AGTTCTTCTA | CATCTTATTA
GTAGAATAAT | | | |

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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)



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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

pCAL0-2:

BsrGI

CGTTAAATTT GCAATTTAAA TTAAAATTCG AATTTAAGC TAATATTTTG ATTATAAAAC TTGTAAACGT AACATTTGCA GTACATGAAA CATGTACTTT

CCGTTTTAGG GGCAAAATCC GGCCGAAATC CCGGCTTTAG TTAACCAATA AATTGGTTAT AGCTCATTTT TCGAGTAAAA AACAATTTAG TTGTTAAATC 51

ACAAGGTCAA TGTTCCAGTT ACCGAGATAG GGTTGAGTGT CCAACTCACA TGGCTCTATC AAAAGAATAG TTTTCTTATC CTTATAAATC GAATATTTAG 101

GACTCCAACG CTGAGGTTGC AAAGAACGTG TTTCTTGCAC GTCCACTATT CAGGTGATAA TGGAACAAGA ACCTTGTTCT

TCAAAGGGCG

TCACCCTAAT AGTGGGATTA ACGAGAACCA TGCTCTTGGT ATGGCCCACT TACCGGGTGA TATCAGGGCG ATAGTCCCGC AAAACCGTC TTTTGGCAG 201

GAACCCTAAA CTTGGGATTT CACTAAATCG GTGATTTAGC TGCCGTAAAG ACGGCATTTC GGGGTCGAGG CCCCAGCTCC CAAGTTTTTT GTTCAAAAA 251

BanII

GGAGCCCCC GATTTAGAGC TTGACGGGGA AAGCCGGCGA ACGTGGCGAG 301

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| igure 35a | : Functional | Figure 35a: Functional maps and sequences of add CCTCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG | Idditional pCAL vector modules and pCAL vectors (continued) CTAAATCTCG AACTGCCCT TTC AAGAAAGCGA AAGGAGCGGG CGC' | ales and pCAL vectors (con AACTGCCCCT AAGGAGCGGG | rinued) TrcGGCCGCT CGCTAGGGCG | TGCACCGCTC |
|---------------------------|--------------|--|---|--|-------------------------------|--------------------------|
| | 401 | TTTCCTTCCC | TTCTTTCGCT | TTCCTCGCCC | CCGCCGCGCT | GACCGTTCAC TAATGCGCCG |
| | 451 | ATCGCCAG'I'G
CTACAGGGCG | NheI
~~~~~~
CGTGCTAGCG | GAGTGTATAC
CTCACATATG | TGGCTTACTA | TGTTGGCACT |
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}
H } | | AgeI |
| JLE 26) | 501 | GATGAGGGTG
CTACTCCCAC | TCAGTGAAGT
AGTCACTTCA | GCTTCATGTG
CGAAGTACAC | GCAGGAGAAA
CGTCCTCTTT | AAAGGCTGCA
TTTCCGACGT |
| | 551 | Agel
~~~~~
CCGGTGCGTC
GGCCACGCAG | AGCAGAATAT
TCGTCTTATA | GTGATACAGG | ATATATTCCG
TATATAAGGC | CTTCCTCGCT |
| | 601 | CACTGACTCG | CTACGCTCGG | TCGTTCGACT | GCGCCGAGCG | GAAATGGCTT |

CCGCTGCGCC GGCGACGCGG

TTCAGTCCGA

GAACCCCCCG CTTGGGGGGC

CTGTATGCAC GACATACGTG

GGTTCGACCT

CCAAGCTGGA

951

AAGTĊAGGCT

GCAGTTCGCT CGTCAAGCGA

TTCCGGGTAG AAGGCCCATC

TGACACTCAG

ATTCCACGCC TAAGGTGCGG

CGTTTGTCTC

901

GCAAACAGAG

ACTGTGAGTC

| CTTTACCGAA | ACTTAACAGG
TGAATTGTCC | CCGCCCCCCT | GAAACCCGAC
CTTTGGGCTG | CTCCTGCGCT
GAGGACGCGA | GTTATGGCCG | |
|---|--------------------------|--------------------------|--------------------------|--------------------------|---|---------------------------|
| ntinued)
CGCCGCTCGC | CCAGGAAGAT
GGTCCTTCTA | TCCATAGGCT
AGGTATCCGA | CAGTGGTGGC
GTCACCACCG | TGGCGGCTCC
ACCGCCGAGG | TCATTCCGCT | |
| litional pCAL vector modules and pCAL vectors (continued) GATGCGAGCC AGCAAGCTGA CGCCGCTCGC | CTGGAAGATG | AAGCCGTTTT
TTCGGCAAAA | ACGCTCAAAT
TGCGAGTTTA | CGTTTCCCCC | AgeI
~~~~~
TTTACCGGTG
AAATGGCCAC | |
| Jitional pCAL vector mod | CGGAGATTTC
GCCTCTAAAG | GGCCGCGGCA
CCGGCGCCGT | ACGAAATCTG
TGCTTTAGAC | AGATACCAGG
TCTATGGTCC | TGCCTTTCGG | |
| Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) GTGACTGAGC GATGCGAGCC AGCAAGCTGA CGC | ACGAACGGGG
TGCTTGCCCC | GAAGTGAGAG
CTTCACTCTC | GACAAGCATC | AGGACTATAA
TCCTGATATT | CTCCTGTTCC |)) ; [;) ; ;)) ; ;) |
| 35a: Functional | 651 | 701 | 751 | 801 | 851 | |
| Figure | | | SUBS | 166 / 2 | ET (RULE 28)
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| | 1001 | TTATCCGGTA
AATAGGCCAT | ACTATCGTCT
TGATAGCAGA | TGAGTCCAAC
ACTCAGGTTG | CCGGAAAGAC
GGCCTTTCTG | ATGCAAAAGC
TACGTTTTCG | |
|------------|------|--------------------------|--------------------------|---|--------------------------|--------------------------|--|
| | 1051 | ACCACTGGCA
TGGTGACCGT | GCAGCCACTG | GTAATTGATT
CATTAACTAA | TAGAGGAGTT
ATCTCCTCAA | AGTCTTGAAG
TCAGAACTTC | |
| c | 1101 | TCATGCGCCG | GTTAAGGCTA
CAATTCCGAT | AACTGAAAGG
TTGACTTTCC | ACAAGTTTTA
TGTTCAAAAT | GTGACTGCGC
CACTGACGCG | |
| NIBSTITUTE | 1151 | TCCTCCAAGC | CAGTTACCTC
GTCAATGGAG | GGTTCAAAGA
CCAAGTTTCT | GTTĠGTAGCT
CAACCATCGA | CAGAGAACCT | |
| DUTET (DU | 1201 | ACGAAAAACC
TGCTTTTTGG | GCCCTGCAAG
CGGGACGTTC | SCCCTGCAAG GCGGTTTTTT
CGGGACGTTC CGCCAAAAA | CGTTTTCAGA
GCAAAAGTCT | GCAAGAGATT | |
| T 001 | | | | | | Bglii | |
| | 1251 | ACGCGCAGAC
TGCGCGTCTG | CAAAACGATC
GTTTTGCTAG | TCAAGAAGAT
AGTTCTTCTA | CATCTTATTA | GATCTAGCAC
CTAGATCGTG | |
| | 1301 | CAGGCGTTTA
GTCCGCAAAT | AGGGCACCAA | TAACTGCCTT
ATTGACGGAA | AAAAAATTA
TTTTTTAAT | 2228222222 | |

| | EEFC |
|---|--------------------------------|
| ontinued) | E |
| ال vectors (در | 1 |
| wles and p ${\mathcal C}$ | PEE FOO F FEE FOREIGN THE TENT |
| vector mod | |
| Iditional pCAL | |
| uences of ad | |
| a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (contin | |
| a: Functional | |
| Figure 35 | |
| | |

| TGCCGACATG | GGCATCAGCA | GGGGCGAAG | AACTCACCCA | TTAGGGAAAT | TATGTGTAGA | AAAACGTTTC | TCCCATATCA |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------|------------|--------------------------|
| ACGGCTGTAC | CCGTAGTCGT | CCCCCGCTTC | TTGAGTGGGT | AATCCCTTTA | ATACACATCT | TTTTGCAAAG | AGGGTATAGT |
| TTAAGCATTC | AATCGCCAGC | TAGTGAAAAC | AAACTGGTGA | AATAAACCCT | CTTGCGAATA | CAGAGCGATG | GTGAACACTA |
| AATTCGTAAG | TTAGCGGTCG | ATCACTTTTG | TTTGACCACT | TTATTTGGGA | GAACGCTTAT | GTCTCGCTAC | |
| TTGTAATTCA
AACATTAAGT | GATGAACCTG
CTACTTGGAC | TATTTGCCCA
ATAAACGGGT | GTTTAAATCA
CAAATTTAGT | ACATATTCTC
TGTATAAGAG | CACGCCACAT | GTATTCACTC | TGTAACAAGG
ACATTGTTCC |
| CGCAGTACTG | CAAACGGCAT | TTGCGTATAA | TATTGGCTAC | GAGACGAAAA | TTCACCGTAA | AATCGTCGTG | TGGAAAACGG |
| GCGTCATGAC | | AACGCATATT | ATAACCGATG | CTCTGCTTTT | AAGTGGCATT | TTAGCAGCAC | ACCTTTTGCC |
| TGCCACTCAT | GAAGCCATCA | CCTTGTCGCC | AAGTTGTCCA | GGGATTGGCT | AGGCCAGGTT | AACTGCCGGA | AGTTTGCTCA |
| ACGGTGAGTA | CTTCGGTAGT | GGAACAGCGG | TTCAACAGGT | CCCTAACCGA | TCCGGTCCAA | TTGACGGCCT | TCAAACGAGT |
| 1351 | 1401 | 1451 | 1501 | 1551 | 1601 | 1651 | 1701 |
|) | | | SUBSTIT | UTE SHEET | (RULE 26) | | |

GACGTCTAAT

AACCTCACCC

TGAAAGTTGG

TTCATTATGG

GTGATCTTAT

2051

| AGCATTCATC
TCGTAAGTAG | GCTTATTTT
CGAATAAAAA | GTCTGGTTAT
CAGACCAATA | TTTACGATGC | TCTCCATTTT
AGAGGTAAAA | ACGCCCGGTA
TGCGGGCCAT | Aatii |
|--|------------------------------|------------------------------|------------------------------|------------------------------|-----------------------------|-------|
| CCGGGTG | TAAAACTTGT G
ATTTTGAACA C | CAGCTGAACG G
GTCGACTTGC C | CAAAATGTTC T
GTTTTACAAG A | GTGATTTTTT T
CACTAAAAAA A | CTCAAAAAT A
GAGTTTTTTA T | |
| additional pCAL vector modules and pCAL vectors (continued) GTCTTTCATT GCCATACGGA ACT(CAGAAAGTAA CGGTATGCCT TGA(| AAAGGCCGGA | CCGTAATATC
GGCATTATAG | TGAAATGCCT
ACTTTACGGA | GGTATATCCA
CCATATAGGT | ATCTCGATAA
TAGAGCTATT | · |
| ditional pCAL vector modi
GTCTTTCATT
CAGAAAGTAA | GAATGTGAAT
CTTACACTTA | TTTAAAAAGG
AAATTTTTCC | AGCAACTGAC
TCGTTGACTG | TATCAACGGT
ATAGTTGCCA | GCTCCTGAAA
CGAGGACTTT | |
| Figure 35a: Functional maps and sequences of ad 1751 CCAGCTCACC GGTCGAGTGG | AGGCGGGCAA
TCCGCCCGTT | CTTTACGGTC | AGGTACATTG
TCCATGTAAC | CATTGGGATA
GTAACCCTAT | AGCTTCCTTA
TCGAAGGAAT | |
| e 35a: Functional
1751 | 1801 | 1851 | 1901 | 1951 | 2001 | ٠ |
| Figun | | | 3003111 | UTE SHEET (
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CTGCAGATTA TTATGCTTCC GIGAGITAGC TCACTCATTA GGCACCCCAG GCTTTACACT TTGGAGTGGG ACTTTCAACC AAGTAATACC CACTAGAATA 2101

| | | *** | | | | | | | |
|--|--------------------------|------|--------------------------|---------|--------------------------|----------|--------------------------|-------------|---|
| AATACGAAGG | CACACAGGAA
GTGTGTCCTT | Sphi | CGCATGCCAT | | CCTGTGAAGT
GGACACTTCA | PacI | GTTTAATTAA
CAAATTAATT | | TCCTTTGATC
AGGAAACTAG |
| ntinued)
CGAAATGTGA | ATAACAATTT
TATTGTTAAA | | ACCCCCCCCC
TGGGGGGGGG | HindIII | ATAAGCTTGA
TATTCGAACT | | TTTGTCTGCC
AAACAGACGG | | CTCAAGAAGA
GAGTTCTTCT |
| dditional pCAL vector modules and pCAL vectors (continued) AGTGAGTAAT CCGTGGGGTC CGA | TTGTGAGCGG | XbaI | GAATTTCTAG | | ATACGAAGTT
TATGCTTCAA | | CGACATTTTT
GCTGTAAAAA | | CAAAAAGGAT
GTTTTTCCTA |
| ditional pCAL vector mod
AGTGAGTAAT | TTGTGTGGAA | | CCATGATTAC
GGTACTAATG | | AATGTACGCT
TTACATGCGA | | GCAGATTGTG
CGTCTAACAC | eI | CGGCCATTAT
GCCGGTAATA |
| Figure 35a: Functional maps and sequences of ad
CACTCAATCG | GGCTCGTATG | | ACAGCTATGA
TGTCGATACT | | AACTTCGTAT
TTGAAGCATA | | GAAAAATGGC
CTTTTTACCG | ·
·
· | 9000000000
000000000000000000000000000 |
| 5a: Functional | 2151 | | 2201 | | 2251 | | 2301 | | 2351 |
| igure 3! | , | | S | | TE SHEET | (RULE 26 | S) | | |
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| | • | | | | | | |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------|------------|
| GTTAAGGGAT | CTTTTAAATT | AACTTGGTCT | GCGATCTGTC | GATAACTACG | TACCGCGAGA | CCAGCCGGAA | CATCCAGTCT |
| CAATTCCCTA | GAAAATTTAA | TTGAACCAGA | CGCTAGACAG | CTATTGATGC | | GGTCGGCCTT | GTAGGTCAGA |
| GAAAACTCAC | CACCTAGATC | TATATGAGTA | ACCTATCTCA | CCGTCGTGTA | GCTGCAATGA | AATAAACCAG | TATCCGCCTC |
| CTTTTGAGTG | GTGGATCTAG | ATATACTCAT | TGGATAGAGT | GGCAGCACAT | | TTATTTGGTC | ATAGGCGGAG |
| TCAGTGGAAC | AAAGGATCTT | ATCTAAAGTA | TCAGTGAGGC | GCCTGACTCC | TGGCCCCCAGT | ATTTATCAGC | CCTGCAACTT |
| AGTCACCTTG | TTTCCTAGAA | TAGATTTCAT | | CGGACTGAGG | ACCGGGGGTCA | TAAATAGTCG | GGACGTTGAA |
| GGTCTGACGC | AGATTATCAA | TTTTAAATCA | CAATGCTTAA | ATCCATAGTT | GCTTACCATC | CCGGCTCCAG | CAGAAGTGGT |
| CCAGACTGCG | TCTAATAGTT | AAAATTTAGT | GTTACGAATT | TAGGTATCAA | CGAATGGTAG | GGCCGAGGTC | GTCTTCACCA |
| TTTTCTACGG
AAAAGATGCC | TTTGGTCATG
AAACCAGTAC | AAAAATGAAG
TTTTTACTTC | GACAGTTACC
CTGTCAATGG | TATTTCGTTC
ATAAAGCAAG | ATACGGGAGG
TATGCCCTCC | CCCACGCTCA | GGGCCGAGCG |
| 2401 | 2451 | 2501 | 2551 | 2601 | 2651 | 2701 | 2751 |
| | | S | UBSTITUTE | SHEET (RUL | E 26) | | |

Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| | | • | | | | | |
|--------------------------|--------------------------|--------------------------|---------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| TTAATAGTTT
AATTATCAAA | CGCTCGTCGT
GCGAGCAGCA | GCGAGTTACA
CGCTCAATGT | GTCCTCCGAT
CAGGAGGCTA | GTTATGGCAG
CAATACCGTC | CTTTTCTGTG | TGCGGCGACC | CCACATAGCA
GGTGTATCGT |
| AGTTCGCCAG
TCAAGCGGTC | CGTGGTGTCA
GCACCACAGT | AACGATCAAG
TTGCTAGTTC | AGCTCCTTCG
TCGAGGAAGC | ATCACTCATG
TAGTGAGTAC | CCGTAAGATG
GGCATTCTAC | GAATAGTGTA
CTTATCACAT | TAATACCGCG |
| TAGAGTAAGT
ATCTCATTCA | CTACAGGCAT
GATGTCCGTA | TCCGGTTCCC | AAAAGCGGTT
TTTTCGCCAA | CCGCAGTGTT
GGCGTCACAA | GTCATGCCAT | GTCATTCTGA
CAGTAAGACT | CAATACGGGA
GTTATGCCCT |
| GCCGGGAAGC | GTTGCCATTG
CAACGGTAAC | TTCATTCAGC
AAGTAAGTCG | TGTTGTGCAA
ACAACACGTT | AGTAAGTTGG
TCATTCAACC | TTCTCTTACT | ACTCAACCAA
TGAGTTGGTT | TGCCCGGCGT
ACGGGCCGCA |
| ATTAACTGTT
TAATTGACAA | GCGCAACGTT | TTGGTATGGC
AACCATACCG | TGATCCCCCA
ACTAGGGGGGT | CGTTGTCAGA
GCAACAGTCT | CACTGCATAA
GTGACGTATT | ACTGGTGAGT
TGACCACTCA | GAGTTGCTCT
CTCAACGAGA |
| 2801 | 2851 | 2901 | 2951 | 3001 | 3051 | 3101 | 3151 |
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

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|---|----------------------------|------------|----------------------------------|---|--|--|
| GCGAAAACTC | CCACTCGCGC | TCTGGGTGAG | GGCGACACGG | GAAGCATTTA | | |
| CGCTTTTGAG | GGTGAGCGCG | AGACCCACTC | CCGCTGTGCC | CTTCGTAAAT | | |
| AGTGCTCATC ATTGGAAAAC GTTCTTCGGG GCGAAAACTC | TCGATGTAAC | CACCAGCGTT | AAGGCAAAAT GCCGCAAAAA AGGGAATAAG | CAATATTATT | | |
| TCACGAGTAG TAACCTTTTG CAAGAAGCCC CGCTTTTGAG | AGCTACATTG | GTGGTCGCAA | TTCCGTTTTA CGGCGTTTTT TCCCTTATTC | GTTATAATAA | | |
| ATTGGAAAAC | GAGATCCAGT | CTTTTACTTT | GCCGCAAAAA | TACTCATACT CTTCCTTTTT CAATATTATT ATGAGTATGA GAAGGAAAAA GTTATAATAA | | |
| TAACCTTTTG | CTCTAGGTCA | GAAAATGAAA | CGGCGTTTTT | | | |
| AGTGCTCATC | TACCGCTGTT | TCCTCAGCAT | AAGGCAAAAT | TACTCATACT | | |
| TCACGAGTAG | ATGGCGACAA | AGGAGTCGTA | TTCCGTTTTA | | | |
| GAACTTTAAA | TCAAGGATCT | ACCCAACTGA | CAAAAACAGG | AAATGTTGAA | | |
| CTTGAAATTT | AGTTCCTAGA | TGGGTTGACT | GTTTTTGTCC | TTTACAACTT | | |
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TCAGGGTTAT TGTCTCATGA GCGGATACAT ATTTGAAT AGTCCCAATA ACAGAGTACT CGCCTATGTA TAAACTTA AGTCCCAATA ACAGAGTACT 3451

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CCTGTGAAGT

ATAAGCTTGA TATTCGAACT

AACTTCGTAT AATGTACGCT ATACGAAGTT TTGAAGCATA TTACATGCGA TATGCTTCAA

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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| AatII | TTAT GACGTCTAAT
AATA CTGCAGATTA | TCACTCATTA GGCACCCCAG GCTTTACACT TTATGCTTCC
AGTGAGTAAT CCGTGGGGTC CGAAATGTGA AATACGAAGG | TTGTGAGCGG ATAACAATTT CACACAGGAA
AACACTCGCC TATTGTTAAA GTGTGTCCTT | SphI | ACCCCCCCC CGCATGCCAT
TGGGGGGGG GCGTACGGTA |
|-------------------|--|--|--|------|--|
| | ACGAAGTTAT
TGCTTCAATA | GCTTTA
CGAAAT | ATAACAATTT
TATTGTTAAA | . ? | ACCCCC
TGGGGG |
| | TGTATGCTAT ACGAAGTTAT
ACATACGATA TGCTTCAATA | GGCACCCCAG
CCGTGGGGGTC | TTGTGAGCGG | XbaI | GAATTTCTAG ACCCCCCCC
CTTAAAGATC TGGGGGGGG |
| | CTTCGTATAA
GAAGCATATT | TCACTCATTA
AGTGAGTAAT | TTGTGTGGAA
AACACACCTT | | CCATGATTAC
GGTACTAATG |
| pCALO-3:
BglII | GATCTCATAA
CTAGAGTATT | GTGAGTTAGC
CACTCAATCG | GGCTCGTATG
CCGAGCATAC | | ACAGCTATGA
TGTCGATACT |
| pCAL | ⊢ | 51 | 101 | | 151 |
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| GTTTAATTAA
CAAATTAATT | | TCCTTTGATC
AGGAAACTAG | GTTAAGGGAT
CAATTCCCTA | CTTTTAAATT
GAAAATTTAA | AACTTGGTCT
TTGAACCAGA | GCGATCTGTC
CGCTAGACAG | GATAACTACG
CTATTGATGC |
|--------------------------|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| TTTGTCTGCC | | CTCAAGAAGA
GAGTTCTTCT | GAAAACTCAC
CTTTTGAGTG | CACCTAGATC
GTGGATCTAG | TATATGAGTA
ATATACTCAT | ACCTATCTCA | CCGTCGTGTA
GGCAGCACAT |
| CGACATTTTT
GCTGTAAAAA | | CAAAAAGGAT
GTTTTTCCTA | TCAGTGGAAC
AGTCACCTTG | AAAGGATCTT
TTTCCTAGAA | ATCTAAAGTA
TAGATTTCAT | TCAGTGAGGC
AGTCACTCCG | GCCTGACTCC
CGGACTGAGG |
| GCAGATTGTG
CGTCTAACAC | eI | CGGCCATTAT
GCCGGTAATA | GGTCTGACGC
CCAGACTGCG | AGATTATCAA
TCTAATAGTT | TTTTAAATCA
AAAATTTAGT | CAATGCTTAA
GTTACGAATT | ATCCATAGTT
TAGGTATCAA |
| GAAAAATGGC
CTTTTTACCG | FSE | | TTTTCTACGG
AAAAGATGCC | TTTGGTCATG
AAACCAGTAC | AAAAATGAAG
TTTTTACTTC | GACAGTTACC
CTGTCAATGG | TATTTCGTTC
ATAAAGCAAG |
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| Figure 35a: Functional maps and sequences of addit | • |

| S.F. | AA
I'T | CT
GA | TT
AA | GT | CA
GT | AT
TA | AG |
|----------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| TACCGCGAGA | CCAGCCGGAA
GGTCGGCCTT | CATCCAGTCT
GTAGGTCAGA | TTAATAGTTT
AATTATCAAA | CGCTCGTCGT | GCGAGTTACA | GTCCTCCGAT | GTTATGGCAG
CAATACCGTC |
| GCTGCAATGA
CGACGTTACT | AATAAACCAG
TTATTTGGTC | TATCCGCCTC | AGTTCGCCAG
TCAAGCGGTC | CGTGGTGTCA | AACGATCAAG
TTGCTAGTTC | AGCTCCTTCG
TCGAGGAAGC | ATCACTCATG
TAGTGAGTAC |
| TGGCCCCCAGT
ACCGGGGGTCA | ATTTATCAGC
TAAATAGTCG | CCTGCAACTT
GGACGTTGAA | TAGAGTAAGT
ATCTCATTCA | CTACAGGCAT
GATGTCCGTA | TCCGGTTCCC | AAAAGCGGTT
TTTTCGCCAA | CCGCAGTGTT
GGCGTCACAA |
| GCTTACCATC | CCGGCTCCAG | CAGAAGTGGT
GTCTTCACCA | GCCGGGAAGC
CGGCCCTTCG | GTTGCCATTG
CAACGGTAAC | TTCATTCAGC
AAGTAAGTCG | TGTTGTGCAA | AGTAAGTTGG
TCATTCAACC |
| ATACGGGAGG
TATGCCCTCC | CCCACGCTCA
GGGTGCGAGT | GGGCCGAGCG
CCCGGCTCGC | ATTAACTGTT
TAATTGACAA | GCGCAACGTT
CGCGTTGCAA | TTGGTATGGC | TGATCCCCCA | CGTTGTCAGA
GCAACAGTCT |
| 601 | 651 | 701 | 751 | 801 | 851 | 901 | 951 |

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|--|--------------------------|--------------------------|------|---------------------------|--------------------------|--------------------------|---------------------------|------------|
| CTTTTCTGTG
GAAAAGACAC | TGCGGCGACC
ACGCCGCTGG | CCACATAGCA
GGTGTATCGT | | GCGAAAACTC
CGCTTTTGAG | CCACTCGCGC
GGTGAGCGCG | TCTGGGTGAG
AGACCCACTC | GGCGACACGG
CCGCTGTGCC | GAAGCATTTA |
| ntinued)
CCGTAAGATG
GGCATTCTAC | GAATAGTGTA
CTTATCACAT | TAATACCGCG
ATTATGGCGC | | GTTCTTCGGG | TCGATGTAAC
AGCTACATTG | CACCAGCGTT
GTGGTCGCAA | AGGGAATAAG
TCCCTTATTC | CAATATTATT |
| ional pCAL vector modules and pCAL vectors (continued)
TCTCTTACT GTCATGCCAT CCG
AGAGAATGA CAGTACGGTA GGC | GTCATTCTGA
CAGTAAGACT | CAATACGGGA
GTTATGCCCT | ImmX | ATTGGAAAAC
TAACCTTTTTG | GAGATCCAGT
CTCTAGGTCA | CTTTTACTTT
GAAAATGAAA | GCCGCAAAAA
CGGCGTTTTT | CTTCCTTTTT |
| ditional pCAL vector mod
TTCTCTT'ACT
AAGAGAATGA | ACTCAACCAA
TGAGTTGGTT | TGCCCGGCGT | | AGTGCTCATC
TCACGAGTAG | TACCGCTGTT
ATGGCGACAA | TCCTCAGCAT
AGGAGTCGTA | AAGGCAAAAT
TTCCGTTTTTA | TACTCATACT |
| Figure 35a: Functional maps and sequences of additions 1001 CACTGCATAA TAGACGTATT A | ACTGGTGAGT
TGACCACTCA | GAGTTGCTCT
CTCAACGAGA | | GAACTTTAAA
CTTGAAATTT | TCAAGGATCT
AGTTCCTAGA | ACCCAACTGA
TGGGTTGACT | CAAAAACAGG
GTTTTTGTCC | AAATGTTGAA |
| igure 35a: Functional
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1201 | (85
1251 | 1301 | 1351 |
| <u>. </u> | | | | 178 / 20 | J4 | | | |

GTTATAATAA CTTCGTAAAT Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) GAAGGAAAAA TTTACAACTT ATGAGTATGA

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ATTTGAATGT ACATGAAATT TGTACTTTAA TAAACTTACA GCGGATACAT CGCCTATGTA TGTCTCATGA ACAGAGTACT AGTCCCAATA TCAGGGTTAT 1401

GTTAAATCAG CAATTTAGTC TTAAATTTTT AATTTAAAAA AAAATTCGCG TTTTAAGCGC GTAAACGTTA ATATTTTGTT TATAAAACAA CATTTGCAAT 1451

CAAAATCCCT GTTTTAGGGA CCGAAATCGG GGCTTTAGCC AACCAATAGG TTGGTTATCC

CTCATTTTT

1501

GAGTAAAAA

TATAAATCAA ATATTTAGTT GAACAAGAGT CTTGTTCTCA

TTCCAGTTTG

AAGGTCAAAC

TTGAGTGTTG

AACTCACAAC GCTCTATCCC CGAGATAGGG

TTCTTATCTG

AAGAATAGAC

CCACTATTAA

1601

1651

CTCCAACGTC GAGGTTGCAG AGAACGTGGA TCTTGCACCT

TTTGGCAGAT

AAACCGTCTA

AAAGGGCGAA

TTTCCCGCTT GGTGATAATT

TCAAAAACC AGTTTTTGG ACCCTAATCA TGGGATTAGT GAGAACCATC CTCTTGGTAG GGCCCACTAC CCGGGTGATG TCAGGGCGAT AGTCCCGCTA

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| ontinued) ACCCTAAAGG GAGCCCCCGA TGGGATTTCC CTCGGGGGCT | GTGGCGAGAA AGGAAGGGAA | GGCAAGTGTA GCGGTCACGC | ATGCGCCGCT ACAGGGCGCG | TTGGCACTGA TGAGGGTGTC | AgeI | AGGCTGCACC GGTGCGTCAG | TCCTCGCTCA CTGACTCGCT |
|---|--------------------------|--------------------------|--------------------------|--|--------|--------------------------|-----------------------|
| ules and pCAL vectors for CTAAATCGGAGAGATTTAGCCT | GCCGGCGAAC | CTAGGGCGCT
GATCCCGCGA | GCCGCGCTTA | GCTTACTATG | | AGGAGAAAAA
TCCTCTTTTT | ATATTCCGCT |
| Stitional pCAL vector mode CCGTAAAGCA GGCATTTCGT | GACGGGGAAA
CTGCCCCTTT | GGAGCGGGCG
CCTCGCCCGC | CACCACACCC | GTGTATACTG | | TTCATGTGGC
AAGTACACCG | GATACAGGAT |
| Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued) 1701 GGTCGAGGTG CCGTAAAGCA CTAAATCGGA ACC(CCAGCTCCAC GGCATTTCGT GATTTAGCCT TGG(| TTTAGAGCTT
AAATCTCGAA | GAAAGCGAAA
CTTTCGCTTT | TGCGCGTAAC
ACGCGCATTG | NheI
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TGCTAGCGGA
ACGATCGCCT | I rumX | AGTGAAGTGC
TCACTTCACG | CAGAATATGT |
| Figure 35a: Functional 1701 | 1751 | 1801 | 1821 | 10
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Figure 35a: Functional maps and sequences of additional pCAL vector modules and pCAL vectors (continued)

| 2051 | ACGCTCGGTC
TGCGAGCCAG | GTTCGACTGC
CAAGCTGACG | GGCGAGCGGA | AATGGCTTAC
TTACCGAATG | GAACGGGGCG |
|------|--------------------------|---------------------------|---------------------------|--------------------------|--------------------------|
| 2101 | GAGATTTCCT
CTCTAAAGGA | GGAAGATGCC
CCTTCTACGG | AGGAAGATAC
TCCTTCTATG | TTAACAGGGA
AATTGTCCCT | AGTGAGAGGG
TCACTCTCCC |
| 2151 | CCGCGGCAAA | GCCGTTTTTC
CGGCAAAAAG | CATAGGCTCC
GTATCCGAGG | GCCCCCCTGA
CGGGGGGACT | CAAGCATCAC
GTTCGTAGTG |
| 2201 | GAAATCTGAC
CTTTAGACTG | GCTCAAATCA
CGAGTTTAGT | GTGGTGGCGA | AACCCGACAG
TTGGGCTGTC | GACTATAAAG
CTGATATTTC |
| 2251 | ATACCAGGCG
TATGGTCCGC | TTTCCCCCTG
AAAGGGGGGAC | GCGGCTCCCT | CCTGCGCTCT
GGACGCGAGA | CCTGTTCCTG
GGACAAGGAC |
| | | AgeI | | | |
| 2301 | CCTTTCGGTT
GGAAAGCCAA | TACCGGTGTC
ATGGCCACAG | ATTCCGCTGT.
TAAGGCGACA | TATGGCCGCG | TTTGTCTCAT
AAACAGAGTA |
| 2351 | TCCACGCCTG | ACACTCAGTT
TGTGAGTCAA | CCGGGTAGGC | AGTTCGCTCC
TCAAGCGAGG | AAGCTGGACT |

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| 2401 | GTATGCACGA | ACCCCCCGTT
TGGGGGGCAA | CAGTCCGACC
GTCAGGCTGG | ACCCCCGTT CAGTCCGACC GCTGCGCCTT ATCCGGTAAC
TGGGGGGCAA GTCAGGCTGG CGACGCGGAA TAGGCCATTG | ATCCGGTAAC
TAGGCCATTG | |
|------|--------------------------|--------------------------|--------------------------|--|--------------------------|--|
| 2451 | TATCGTCTTG
ATAGCAGAAC | AGTCCAACCC
TCAGGTTGGG | GGAAAGÄCAT
CCTTTCTGTA | AGTCCAACCC GGAAAGACAT GCAAAAGCAC CACTGGCAGC
TCAGGTTGGG CCTTTCTGTA CGTTTTCGTG GTGACCGTCG | CACTGGCAGC | |
| 2501 | AGCCACTGGT
TCGGTGACCA | AATTGATTTA
TTAACTAAAT | GAGGAGTTAG
CTCCTCAATC | AATTGATTTA GAGGAGTTAG TCTTGAAGTC ATGCGCCGGT
TTAACTAAAT CTCCTCAATC AGAACTTCAG TACGCGGCCA | ATGCGCCGGT | |

BglII

AAAAGTCTCG

GGTTTTTTCG

GGACGTTCCG

CCTGCAAGGC

2651

TTTTCAGAGC

2701 AAACGATCTC AAGAAGATCA TCTTATTA TTTGCTAGAG TTCTTCTAGT AGAATAAT

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2601

GAGGTTCGGT

CTGACGCGAG

TTCAAAATCA

GACTTTCCTG

ATTCCGATTT

TAAGGCTAAA

2551

CTGAAAGGAC

AAGTTTTAGT

GACTGCGCTC

CTCCAAGCCA

CTTTTTGGCG

CTCTTGGATG

ACCATCGAGT

AAGTTTCTCA

CAATGGAGCC

GTTACCTCGG

GAGAACCTAC

TTCAAAGAGT TGGTAGCTCA

GAAAAACCGC

GCGCAGACCA

AAGAGATTAC TTCTCTAATG Figure 35b: List of oligonucleotides used for synthesis of modules

M1: PCR using template

NoVspAatII: TAGACGTC

M2: synthesis

BloxA-A: TATGAGATCTCATAACTTCGTATAATGTACGCTATACG-

AAGTTAT

BloxA-B: TAATAACTTCGTATAGCATACATTATACGAAGTTATG-

AGATCTCA

M3: PCR, NoVspAatll as second oligo

XloxS-muta: CATTTTTGCCCTCGTTATCTACGCATGCGATAACTTCGTA-

TAGCGTACATTATACGAAGTTATTCTAGACATGGTCATAGCTGTTTCCTG

M7-1: PCR

gIIINEW-fow: GGGGGGAATTCGGTGGTGGTGGATCTGCGTGCGCTG-

AAACGGTTGAAAGTTG

gIIINEW-rev: CCCCCCAAGCTTATCAAGACTCCTTATTACG

M7-II: PCR

glllss-fow: GGGGGGGAATTCGGAGGCGGTTCCGGTGGTCGC

M7-III: PCR

glllsupernew-fow: GGGGGGGAATTCGAGCAGAAGCTGATCTCT-

GAGGAGGATCTGTAGGGTGGTGGCTCTGGTTCCGGTGATTTTG

Figure 35b: List of oligonucleotides used for synthesis of modules (continued)

M8: synthesis

Iox514-A: CCATAACTTCGTATAATGTACGCTATACGAAGTTATA

Iox514-B: AGCTTATAACTTCGTATAGCGTACATTATACGAAGT-

TATGGCATG

M9II: synthesis

M9II-fow: AGCTTGACCTGTGAAGTGAAAAATGGCGCAGATT-

M9II-rev: GTACACCCCCCCCAGGCCGGCCCCCCCCCCTTTAA-

TTAAACGGCAGACAAAAAAAAATGTCGCACAATCTGCG

M10II: assembly PCR with template

bla-fow: GGGGGGGTGTACATTCAAATATGTATCCGCTCATG

bla-seq4: GGGTTACATCGAACTGGATCTC

bla1-muta: CCAGTTCGATGTAACCCACTCGCGCACCCAACTGATC-

CTCAGCATCTTTTACTTTCACC

blall-muta: ACTCTAGCTTCCCGGCAACAGTTAATAGACTGGATG-

GAGGCGG

bla-NEW: CTGTTGCCGGGAAGCTAGAGTAAG

bla-rev: CCCCCCTTAATTAAGGGGGGGGGCCGGCCATTATCAAA-

AAGGATCTCAAGAAGATCC

M11II/III: PCR, site-directed mutagenesis

Figure 35b: List of oligonucleotides used for synthesis of modules (continued)

f1-fow: GGGGGGGCTAGCACGCCCCTGTAGCGGCGCATTAA

f1-rev: CCCCCCTGTACATGAAATTGTAAACGTTAATATTTTG

f1-t133.muta: GGGCGATGGCCCACTACGAGAACCATCACCCTAATC

M12: assembly PCR using template

p15-fow: GGGGGGAGATCTAATAAGATGATCTTCTTGAG

p15-NEWI: GAGTTGGTAGCTCAGAGAACCTACGAAAAACCGCCCTG-

CAAGGCG

p15-NEWII: GTAGGTTCTCTGAGCTACCAACTC

p15-NEWIII: GTTTCCCCCTGGCGCTCCCTCCTGCGCTCTCCTGTTCCT-

GCC

p15-NEWIV: AGGAGGGAGCCGCCAGGGGGAAAC

p15-rev: GACATCAGCGCTAGCGGAGTGTATAC

M13: synthesis

BloxXB-A: GATCTCATAACTTCGTATAATGTATGCTATACGAAGTTA-

TTCA

BloxXB-B: GATCTGAATAACTTCGTATAGCATACATTATACGAAGTTA-

TGAGA

M14-Ext2: PCR, site-directed mutagenesis

Colext2-fow: GGGGGGGAGATCTGACCAAAATCCCTTAACGTGAG

Col-mutal: GGTATCTGCGCTCTGCTGTAGCCAGTTACCTTCGG

Figure 35b: List of oligonucleotides used for synthesis of modules (continued)

Col-rev: CCCCCCGCTAGCCATGTGAGCAAAAGGCCAGCAA

M17: assembly PCR using template

CAT-1: GGGACGTCGGGTGAGGTTCCAAC

CAT-2: CCATACGGAACTCCGGGTGAGCATTCATC

CAT-3: CCGGAGTTCCGTATGG

CAT-4: ACGTTTAAATCAAAACTGG

CAT-5: CCAGTTTTGATTTAAACGTAGCCAATATGGACAACTTCTTC-

GCCCCGTTTTCACTATGGGCAAATATT

CAT-6: GGAAGATCTAGCACCAGGCGTTTAAG

M41: assembly PCR using template

LAC1: GAGGCCGGCCATCGAATGGCGCAAAAC

LAC2: CGCGTACCGTCCTCATGGGAGAAAATAATAC

LAC3: CCATGAGGACGGTACGCGACTGGGCGTGGAGCATCTGGTCGCA-

TTGGGTCACCAGCAAATCCGCTGTTAGCTGGCCCATTAAG

LAC4: GTCAGCGGCGGGATATAACATGAGCTGTCCTCGGTATCGTCG

LAC5: GTTATATCCCGCCGCTGACCACCATCAAAC

LAC6: CATCAGTGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGT4TTG-

GGAGCCAGGGTGGTTTTTC

LAC7: GGTTAATTAACCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCC-

AGCTGCATCAGTGAATCGGCCAAC

M41-MCS-fow: CTAGACTAGTGTTTAAACCGGACCGGGGGGGGGCTT-

AAGGGGGGGGGGG

Figure 35b: List of oligonucleotides used for synthesis of modules (continued)

M41-MCS-rev: CTAGCCCCCCCCCCCTTAAGCCCCCCCCGGTCCGGT-

TTAAACACTAGT

M41-fow: CTAGACTAGTGTTTAAACCGGACCGGGGGGGGGGCTTAA-

GGGGGGGGGGG

M41-rev: CCCCCCTTAAGTGGGCTGCAAAACAAACGGCCTCC-

TGTCAGGAAGCCGCTTTTATCGGGTAGCCTCACTGCCCGCTTTCC

M41-A2: GTTGTTGTGCCACGCGGTTAGGAATGTAATTCAGCTCCGC

M41-B1: AACCGCGTGGCACAACAAC

M41-B2: CTTCGTTCTACCATCGACACGACCACGCTGGCACCCAGTTG

M41-C1: GTGTCGATGGTAGAACGAAG

M41-CII: CCACAGCAATAGCATCCTGGTCATCCAGCGGATAGTT-

AATAATCAGCCCACTGACACGTTGCGCGAG

M41-DI: GACCAGGATGCTATTGCTGTGG

M41-DII: CAGCGCGATTTGCTGGTGGCCCAATGCGACCAGATGC

M41-EI: CACCAGCAAATCGCGCTG

M41-EII: CCCGGACTCGGTAATGGCACGCATTGCGCCCAGCGCC

M41-FI: GCCATTACCGAGTCCGGG

M42: synthesis

Eco-H5-Hind-fow: AATTCCACCATCACCATTGACGTCTA

Fco-H5-Hind-rev: AGCTTAGACGTCAATGGTGATGATGGTGG

Figure 36: functional map and sequence of ß-lactamase-MCS module

| Bbe I (1361) Ase I (1364) Eco 57I (1366) Xho I (1371) Bss HII (1376) Bbs I (1386) Bsp EI (1397) Bsr GI (1403) | |
|--|----------------------------|
| Bam H I (192) Pst I (1356) Kpn I (202) Bss SI (1346) Fsc I (210) Eag I (1340) -35 (bla) bla-term bla-term | bla MCS
1289 bp |
| Pml 1 (189) Bsa Bl (182) Nsp V (173) Bsi Wl (166) Eco O109l (161) Psp 5ll (161) Sty I (157) Msc I (156) Bst XI (152) Bst Ell (140) Bsu 36l (136) | Hpa I (132)
Mlu I (126) |

CTCAGTGGAA GAGTCACCTT

GGGTCTGACG

CTTTTCTACG GAAAGATGC

ATCCTTTGAT TAGGAAACTA

AGAGTTCTTC

TCTCAAGAAG

226

AAAAGGATCT

GAGATTATCA

CTCTAATAGT

AAAACCAGTA

TTTTGGTCAT

CGTTAAGGGA

CGAAAACTCA

276

GCTTTTGAGT

GCAATTCCCT

TTTCCTAGA

Figure 36: functional map and sequence of B-lactamase-MCS module (continued)

| | | | | | BsiWI NspV | ~ | GTACGTTCGA | CATGCAAGCT | | | | | | TCAAAAAGGA | AGTTTTTCCT |
|--|--------|-------------|--------------|---|------------|---|---|----------------------------------|-----|------|------|-----------|---|--|-----------------------|
| $\operatorname{StyI}_{\sim\sim\sim\sim\sim\sim}$ | Psp511 | ? ? ? ? ? ? | Eco01091 | ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ | H | | TCAGGTGACC AAGCCCCTGG CCAAGGTCCC GTACGTTCGA | TTCGGGGACC GGTTCCAGGG CATGCAAGCT | | | | FseI | 2 | AGATTACCAT CACGTGGATC CGGTACCAGG CCGGCCATTA TCAAAAAGGA | GCCATGGTCC GGCCGGTAAT |
| | | | BstXI | 2 | MscI | 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | AAGCCCCTGG | TTCGGGGACC | | | | KpnI | | CGGTACCAGG | GCCATGGTCC |
| | | | 36I | | BStEII | 2 | TCAGGTGACC | AGTCCACTGG | | PmlI | **** | BamHI | ~ ~ ~ ~ ~ ~ ~ | CACGTGGATC | GTGCACCTAG |
| | | | MluI. Bsu36I | ~ | HpaI | 2 2 2 2 2 | Ŋ | GCGCAATTGG | | | | NspVBsaBI | 1 | AGATTACCAT | TCTAATGGTA |
| | | | | | | • | 126 | | | | | | | 176 | |
| | | | | | | | SU | RSTE | TUT | F SH | IEE | T (RU | LE : | 26) | |

Figure 36: functional map and sequence of B-lactamase-MCS module (continued)

| 326 | TCACCTAGAT | CCTTTTAAAT | TAAAAATGAA | GTTTTAAATC | AATCTAAAGT |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| | AGTGGATCTA | GGAAAATTTA | ATTTTTACTT | CAAAATTTAG | TTAGATTTCA |
| 376 | ATATATGAGT | AAACTTGGTC | TGACAGTTAC | CAATGCTTAA | TCAGTGAGGC |
| | TATATACTCA | TTTGAACCAG | ACTGTCAATG | GTTACGAATT | AGTCACTCCG |
| 426 | ACCTATCTCA | GCGATCTGTC | TATTTCGTTC | ATCCATAGTT | GCCTGACTCC |
| | TGGATAGAGT | CGCTAGACAG | ATAAAGCAAG | TAGGTATCAA | CGGACTGAGG |
| 476 | CCGTCGTGTA | GATAACTACG
CTATTGATGC | ATACGGGAGG
TATGCCCTCC | GCTTACCATC
CGAATGGTAG | TGGCCCCCAGT |
| 526 | GCTGCAATGA
CGACGTTACT | TACCGCGAGA | CCCACGCTCA
GGGTGCGAGT | CCGGCTCCAG
GGCCGAGGTC | ATTTATCAGC
TAAATAGTCG |
| 576 | AATAAACCAG | CCAGCCGGAA | GGGCCGAGCG | CAGAAGTGGT | CCTGCAACTT |
| | TTATTTGGTC | GGTCGGCCTT | CCCGGCTCGC | GTCTTCACCA | GGACGTTGAA |
| 929 | TATCCGCCTC
ATAGGCGGAG | CATCCAGTCT | ATTAACTGTT
TAATTGACAA | GCCGGGAAGC | TAGAGTAAGT
ATCTCATTCA |
| 919 | AGTTCGCCAG
TCAAGCGGTC | TTAATAGTTT
AATTATCAAA | GCGCAACGTT
CGCGTTGCAA | GTTGCCATTG | CTACAGGCAT
GATGTCCGTA |

Figure 36: functional map and sequence of B-lactamase-MCS module (continued)

| TCCGGTTCCC | AAAAGCGGTT | CCGCAGTGTT | GTCATGCCAT | GTCATTCTGA | CAATACGGGA | ATTGGAAAAC | GAGATCCAGT |
|--------------------------|------------|--------------------------|--------------------------|--------------------------|------------|--------------------------|--------------------------|
| | TTTTCGCCAA | GGCGTCACAA | CAGTACGGTA | CAGTAAGACT | GTTATGCCCT | TAACCTTTTG | CTCTAGGTCA |
| TTCATTCAGC
AAGTAAGTCG | TGTTGTGCAA | AGTAAGTTGG
TCATTCAACC | TTCTCTTACT
AAGAGAATGA | ACTCAACCAA
TGAGTTGGTT | TGCCCGGCGT | AGTGCTCATC
TCACGAGTAG | TACCGCTGTT
ATGGCGACAA |
| TTGGTATGGC | TGATCCCCCA | CGTTGTCAGA | CACTGCATAA | ACTGGTGAGT | GAGTTGCTCT | GAACTTTAAA | TCAAGGATCT |
| AACCATACCG | | GCAACAGTCT | GTGACGTATT | TGACCACTCA | CTCAACGAGA | ÇTTGAAATTT | AGTTCCTAGA |
| CGCTCGTCGT | GCGAGTTACA | GTCCTCCGAT | GTTATGGCAG | CTTTTCTGTG | TGCGGCGACC | CCACATAGCA | GCGAAAACTC |
| GCGAGCAGCA | CGCTCAATGT | | CAATACCGTC | GAAAAGACAC | ACGCCGCTGG | GGTGTATCGT | CGCTTTTGAG |
| CGTGGTGTCA | AACGATCAAG | AGCTCCTTCG | ATCACTCATG | CCGTAAGATG | GAATAGTGTA | TAATACCGCG | GTTCTTCGGG |
| | TTGCTAGTTC | TCGAGGAAGC | TAGTGAGTAC | GGCATTCTAC | CTTATCACAT | ATTATGGCGC | CAAGAAGCCC |
| 726 | 176 | 826 | 876 | 926 | 916 | 1026 | 1076 |

Figure 36: functional map and sequence of B-lactamase-MCS module (continued)

| CGTA CALLIACILI
CGTA GAAAATGAAA
I | AAAT GCCGCAAAAA
TTTA CGGCGTTTTT | TACT CTTCCTTTTT
ATGA GAAGGAAAAA | ATGA GCGGATACAT
TACT CGCCTATGTA | XhoI | Asel BssHII | ATTA ATGGCTCGAG
TAAT TACCGAGCTC | |
|---|------------------------------------|------------------------------------|------------------------------------|------------|-------------|------------------------------------|-------------|
| TCTTCAGCAT
AGAAGTCGTA
Eco57I | AAGGCAAAAT
TTCCGTTTTA | TACTCATACT
ATGAGTATGA | TGTCTCATGA
ACAGAGTACT | } | Bbel Asel | GGCGCCATTA | H ~ |
| ACCCAACTGA
TGGGTTGACT | CAAAAACAGG
GTTTTTGTCC | AAATGTTGAA
TTTACAACTT | TCAGGGTTAT | PstI | BssSI | | BspEI BsrGI |
| CCACTCGTGC
GGTGAGCACG
BSSSI | TCTGGGTGAG | GGCGACACGG
CCGCTGTGCC | GAAGCATTTA
CTTCGTAAAT | | 1 | ACTCGGCCGC | |
| TCGATGTAAC
AGCTACATTG | CACCAGCGTT
GTGGTCGCAA | AGGGAATAAG
TCCCTTATTC | CAATATTATT
GTTATAATAA | | • | ATTTGAATGT
TAAACTTACA | BssHII |
| 1126 | 1176 | 1226 | 1276 | | | 1326 | |
| | | יבידט חוו א | TE ALLERS | DI II E 60 | | | |

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| | CATGAAATT | GTACTTTAA | | |
|---|--|--|--------|-------------|
| module (continued) | TCCGGATGTA | AGGCCTACAT | • | ~ . |
| ence of I3-lactamase-MCS | CGCTTTGTCT | GCGAAACAGA | BbsI | 2 2 2 2 2 2 |
| Figure 36: functional map and sequence of 13-lactamase-MCS module (continued) | CGCGCTTCAG CGCTTTGTCT TCCGGATGTA CATGAAATT | GCGCGAAGTC GCGAAACAGA AGGCCTACAT GTACTTTAA | Eco57I | ? ? ? ? |
| Figure 3 | 76 |) | | |

Figure 37: Oligo and primer design for $V\kappa$ CDR3 libraries

| | | | | | | | | | | | 10 | | | | | | | |
|-----------|-----|-------------|---|--------------|---|---|---|---|---|---|----|---|----|---|-----|----|---|----------------|
| 0_K3L_5 | 5'- | G | С | C | C | T | G | C | Α | Α | G | Ċ | GG | Α | Α | G | Α | C |
| | | | | | | | | | | | | | | | Bb | sl | | |
| | | | | | | | | | | | | | | E | | | D | |
| Vk1 & Vk3 | 5'- | G | C | C | C | T | G | C | Α | Α | G | C | GG | Α | Α | G | Α | C |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | Ε | . ' | | D | • |
| Vk2 | 5'- | G | C | C | Ċ | T | G | C | Α | Α | G | Ċ | GG | Α | Α | G | Α | \mathbf{C} |
| | | | | | | | | | | | | | | E | | | D | |
| Vk4 | 5'- | G | C | \mathbf{C} | C | Т | G | C | Α | Α | G | C | GG | A | Α | G | A | \overline{C} |

Figure 37: Oligo and primer design for Vk CDR3 libraries

30 20 -3' . **O** CATTATTGC GCGACITA G CA GGGCG G G CAGGCGGTGTA G Α C D E F G Н CAK M N P CAG R S

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Figure 37: Oligo and primer design for $\mbox{V}\kappa$ CDR3 libraries

 $_{\mathsf{G}}$ A C C T

G A C C T
G A C C T

| | | <u></u> , | | **** | 1 | | | | | | | | | ••••• | | · | : |
|----------|----------|-----------|---|-------------|---|------------|--------------|---------|------------|---|----------|-----------|------------|---------------------------------------|---|---|---|
| G | C | T | | | | | | | G | C | - | | | | G | C | |
| | ******** | 1 | | .,, | | | | | | | | | | | | | İ |
| G | Ā | T | G | A | T | G | Α | Τ | G | Α | T | | | | G | Α | T |
| G | Α | i | | ***** | | ********** | | | G | | | | | | G | Α | G |
| T | T | T | | | | | | | T | T | T | ····· | · | | T | Ţ | T |
| G | G | T | G | G | T | G | G | T | G | G | T | ********* | ••••• | | G | G | T |
| : | Ā | Τ | | | | | | | | Α | T | | ******* | | С | Α | T |
| Α | Ť | T | | | | | | | Α | T | T | | | - | Α | T | T |
| A | A | G | | | | | | | Α | Α | G | ********* | | | Α | Α | G |
| C | T | T | | | | | | | С | T | Τ | | ********* | | С | T | T |
| A | T | G | | | | | | | Α | T | G | ********* | ********** | | Α | T | G |
| Α | Α | T | Α | A | T | Α | Α | T | Α | Α | T | | ********** | 44 5114 | Α | Α | T |
| | | | | | | | | | С | C | T | C | C | T | С | C | T |
| C | Α | G | | | ***** | | | | С | Α | G | | | | C | Α | G |
| C | G | T | | | | | 414-41-1-1-1 | | : | | | • | | | | G | Τ |
| T | C | T | T | С | T | Τ | C | T | T | C | T | T | C | T | Τ | С | T |
| Α | C | T | | | • | | | | Α | C | T | | | | Α | С | T |
| G | T | T | | ••••• | •••••• | | | | G | Ť | T | | | | G | T | T |
| T | G | G | | | • | | | ******* | T | G | G | | | · · · · · · · · · · · · · · · · · · · | T | G | G |
| T | Α | T | T | A | T | | | | T | Α | T | | | | T | Α | T |
| 5 | 0% | Υ | İ | | ••••• | | | •••• | ********** | | ········ | 80 |)% | P |] | | |

Figure 37: Oligo and primer design for $\mbox{V}\kappa$ CDR3 libraries

| | | | | | 70 | | | | | | | | | | 80 | 81 | | |
|---|---|---|---|----------|----|---|---|---|---|---|---|---|---|---|----|----|-----|---------|
| Α | Α | C | С | G | G | T | Α | Α | G | C | T | T | T | C | G | G | -5' | 0_K3L_3 |
| | | | M | scl | | | | | | | | | | | | | | • |
| F | | | G | | | 0 | | | | | | | | | _ | _ | | |
| T | T | G | G | <u>c</u> | C | Α | T | T | C | G | Α | Α | A | G | C | C | -3. | |
| | | | | | | | | | | | | | | | | | | |
| F | | | G | | | Q | | | | | | | | | | | | |
| T | T | G | G | С | С | Α | T | T | C | G | Α | A | Α | G | C | C | -3' | |
| F | | | G | | | Q | | | | | | | | | | | | |
| T | T | G | G | C | C | Α | T | T | C | G | Α | Α | Α | G | C | C | -3' | |

Figure 38: Oligo and primer design for VA CDR3 libraries

E D E A D
5'- C C T G C A A G C G G A A G A G C G G A T T -

Figure 38: Oligo and primer design for VA CDR3 libraries

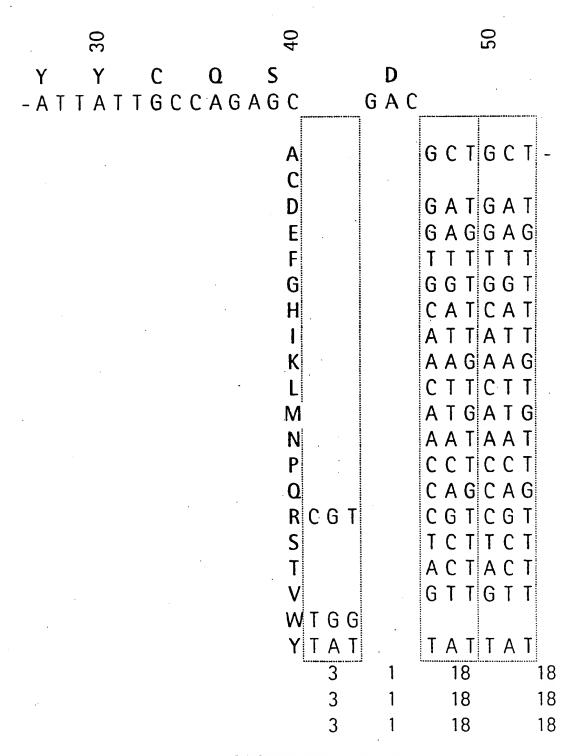


Figure 38: Oligo and primer design for V λ CDR3 libraries

| 09 | | · | 70 | | | | 80 |
|--|-------|----------|-----|-------|-------|-----|-----|
| • | | G G | | G | T | | _ L |
| | G | GGGGG | C G | G C / | A C G | AAG | TTA |
| gap gap | C C T | | | | | | |
| - G C T G C T G C T | U C I | | | | | | |
| GATGATGAT | GAT | | | | | | |
| GAGGAGGAG | G A G | | | | • | | |
| TTTTTTT | TTT | | • | | | | |
| GGTGGTGGT | 1 1 | | | | | | |
| CATCATCAT | 1 1 | | | | | | |
| ATTATTATI | 1 1 | | | | | | |
| AAGAAGAAG | _: | | | | | | |
| C T T C T T C T T
A T G A T G A T G | 1 | | | | | . • | |
| AATAATAAT | 1 | • | | | | | |
| ССТССТССТ | 1 1 | | • | | | | |
| CAGCAGCAG | : ; | | | | | | |
| CGTCGTCG | : ; | | | | | • | , |
| TCTTCTTC | 1 1 | · | | | | | |
| ACTACTAC | 1. : | | | | | | |
| GTTGTTGT | | | | | | | |
| | TGG | | | | | | |
| TATTATTA | TAT | Variabil | ity | | | | |
| 18 | 19 | 3.32E+ | 05 | | | | • |
| 18 18 | 19 | 5.98E+ | 90 | | | | |
| 18 18 18 | 19 | 1.08E+ | 80 | | | | |

Figure 38: Oligo and primer design for VA CDR3 libraries

T V L G Q E F
ACCGTTCTTGGCCAGGAATTCGAGCC-3'
3'-CCGGTCCTTAAGCTCGG-5'

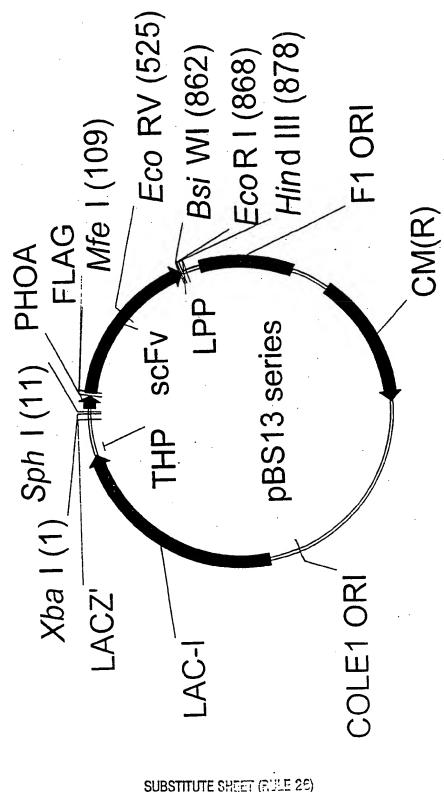


Figure 39: functional map of expression vector series pBS13

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Figure 40: Expression data for HuCAL scFvs (pBS13, 30°C)

| % soluble | К | 7 | $\mathcal{L}_{\mathcal{A}}$ | к4 | 71 | 77 | 73 |
|-----------|-----|-------|-----------------------------|-----|-----|-----|-----|
| H1A | 61% | 58% | 52% | 42% | %06 | 61% | %09 |
| H18 | 39% | 48% | %99 | 48% | 47% | 39% | 36% |
| H2 | 47% | 57% | 46% | 49% | 37% | 36% | 45% |
| H3 | 85% | 9/2/9 | 76% | 61% | 80% | 71% | 83% |
| H4 | %69 | 52% | 51% | 44% | 45% | 33% | 42% |
| Ξ2 | 49% | 49% | 46% | 67% | 54% | 46% | 47% |
| 9H | %06 | 58% | 54% | 47% | 45% | 20% | 51% |

| Total amount | | | | | | (| (|
|------------------|-------|-------|-------------|----------|-------|------------|----------|
| C2C II 04 POWDER | ヹ | Ø | ξ | 4 | ۲۷ | 77 | ۲3 |
| Compared to nonz | 7890% | 940% | 1660% | 2720% | 200% | 150% | 78% |
| 217 | 2190% | 1220% | %054
80% | 1390% | 1170% | 1580% | 1010% |
| 0 LI | 1960% | 2230% | 20800 | 182% | 126% | 60%
60% | 970% |
| 711 | 0,00 | 0/677 | 710% | 102.0 | 50% | 120% | 3/1/6 |
| H3 | 20%0 | i | 0/01/ | 24% | 33%0 | 130%0 | 47.40 |
| H4 | 3/0/0 | 25% | 9/09 | 0/0// | 195% | 0/0/01 | 0/n C7 |
| H5 | %86 | 201% | 167% | 83% | 93% | 128% | 115% |
| H6 | 65% | 117% | 89% | 109% | 299% | 215% | 278% |

Figure 40: Expression data for HuCAL scFvs (pBS13, 30°C)

| Soluble amount | ? | در. | Š | 7. | ٦٦. | 33 | 73 |
|------------------|----------|------|------|--------|------|------|-------|
| compared to H3K2 | Z | 2 | 2 | †
2 | ₹ | 77 | 3 |
| H1A | 191% | 880% | 121% | 122% | 26% | 211% | 76% |
| H1B | 1.24% | 95% | 83% | 107% | 79% | 142% | 29% |
| H2 | 126% | 204% | 139% | 130% | %99 | 20% | 0/0/2 |
| H3 | 63% | ı | 81% | 49% | %69 | 143% | 61% |
| H4 | 40% | 47% | 49% | 54% | 95% | 22% | 125% |
| H5 | %69 | 158% | 116% | 80% | 72% | 84% | 84% |
| 8 9H | 85% | 122% | 87% | 77% | 162% | 162% | 212% |
| | McPC | | | | | | |
| soluble | 38% | | | Ÿ | | | |
| %H3k2 total | 117% | | | | | | |
| %H3k2 soluble | %69 | | | | | | |
| | | | | | | | |